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INTERNAL SECRETIONS

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Hiccup!

From "The Journal" A. M. A., August 21, 1920, page 567

Is Quoted the Following

"Benzyl Benzoate in Hiccup. Macht has found benzyl benzoate to be an invaluable medicine in the treatment of persistent hiccup of both adults and children. Not only has it been found useful in allaying the ordinary mild forms of hiccup so common in infants, but the drug has been found to be efficient in stopping those forms of hiccup termed pernicious, that is, those cases in which the phenomenon persisted for long periods of time, from twenty-four hours to several days, and in which the singultus was unaffected by all other forms of medicinal treatment, both external and internal. . . . Inasmuch as benzyl benzoate exerts its chief effect peripherally on the smooth muscle structures, the author is inclined to believe that this drug may be most useful in the treatment of hiccups of peripheral origin. The benzyl benzoate exerts its action best when given in a 20 per cent solution in alcohol."

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ENDOCRINOLOGY

THE BULLETIN of the ASSOCIATION

for the STUDY of

INTERNAL SECRETIONS

OCTOBER-DECEMBER, 1920

EXPERIMENTAL RESEARCHES ON THE PITUITARY BODY

DIABETES INSIPIDUS, GLYCOSURIA AND THOSE DYSTROPHIES CONSIDERED AS HYPOPHYSEAL IN ORIGIN*

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Professeur, agrégé, a la Faculté de Médicin de Paris

In recent years, notably before the War, we have carried out a series of researches on the pituitary body. These researches, undertaken without any preconceived idea, have furnished some results which have for the most part been published in various journals. It is of these results that we wish now to offer a succinct review.

I. DIABETES INSIPIDUS AND THAT WHICH IS TERMED "HYPOPHYSEAL POLYURIA"

We must consider in succession the relation of polyuria to the removal of the pituitary body, the relation of polyuria to the lesions of the base of the brain, the site of the lesions which lead to polyuria, the interrelation of polyuria and polydipsia and the question of the regulation of water retention in the body.

1. *Polyuria and removal of the pituitary body.* In a very great number of hypophysectomies, partial or total, practised on the dog by the buccal-transpalato-sphenoidal route, we have

*Read before the Association for the Study of Internal Secretions, New Orleans, April 26, 1920.

observed a marked polyuria. We were surprised at the outset of our researches at the copiousness of the polyuria. It even happened in the first two animals we operated upon that we could not measure the urine passed because we had placed under the cage receptacles of from only one to two litres and during the night these overflowed.

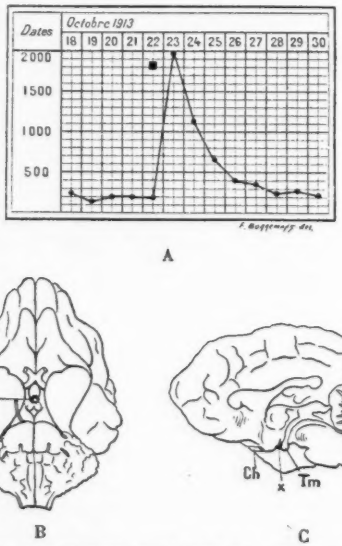


Fig. 1. Female Dog Tigrette (weight 9 k.). Total extirpation of hypophysis Oct. 22, 1913, followed by profuse polyuria. Death, Dec. 26. Autopsy findings: Excoriation and dilation of the tuber at the border of the insertion of the stalk, the stalk itself has been removed; no trace of hypophysis in the sella turcica. On section a small fragment found in the cavity of the infundibulum at the right. The graph A shows the urine volume following operation on the 22nd; B, base of the brain showing infundibulum (If.) dilated; C, right hemisphere, inner surface; Ch, optic chiasma; T.m., mammillary body; X, lesion.

Thinking, at the commencement of our work, that the pituitary body was alone involved, we wished to begin by measuring the relative importance of the different parts of the organ in the production of the phenomena. But we were very rapidly brought to a realization that the key to the phenomenon is not to be found in an attenuation of the hypophyseal function. Contrary to the generally accepted view, these ablations—whether total or limited to one lobe—did not influence diuresis.

There follow, chosen from among the others, two examples which bring out this point. Of two hypophysectomized dogs there appears in the first (Tigrette) complete removal of the hypophysis resulting in a notable polyuria and in the second (Agrippine) a removal equally complete which does not give a trace of polyuria.

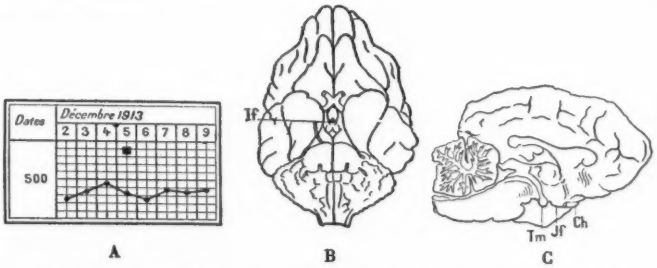


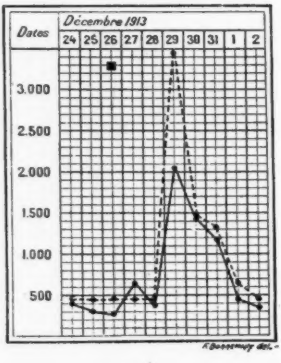
Fig. 2. Female Dog Agrippine (weight 7 k.). Total ablation of hypophysis Dec. 5, 1910. Polyuria followed. Animal killed Apr. 28. Autopsy showed stalk intact, infundibulum intact and not dilated, even constricted. Brain absolutely normal superficially at the base and upon median section. In the sella turcica no trace of hypophyseal tissue. Graph A shows the absence of polyuria; B, base of brain with infundibulum (If.) not altered; C, internal aspect showing integrity of the infundibulum (If.), of the chiasma (Ch.), and of the mammillary body (T.m.).

The autopsies showed that in the first case the base of the brain had been somewhat injured during the hypophysectomy, while in the second the brain was absolutely intact. This brings us to a consideration of our second question.

2. *Polyuria and lesions of the base of the brain.* Later, in evaluating the rôle played by lesions at that part of the base of the brain which borders on the pituitary body, we began injuring this region with a heated needle, meanwhile respecting the hypophysis itself. To do this we perforated the sphenoid with a gimlet. We have performed this operation successfully five times, each time with a very marked consequent polyuria—this despite an absolute lack of any change in the pituitary body, as shown at autopsy (Amilcar and Télémaque).

To exhibit the phenomenon even more evidently, we performed on each of two other dogs (Alexander and Annibal) two operations, separated by an interval of several weeks. In the first operation we removed the pituitary body, which ablation was followed by a passing polyuria. In the second operation, now that the pituitary could not be the cause, we injured the

base of the brain. A polyuria of equal intensity or even more marked than that after the first intervention, made its appearance.



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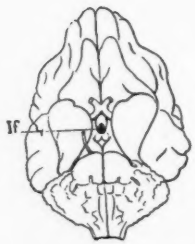

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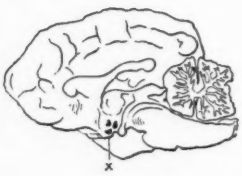

C

Fig. 3. Male Dog Amilcar (weight 11.2 k.). Puncture of the base of the brain Dec. 26, 1913. Following this, elevation of urinary output surpassing ingested water, which demonstrates that the polyuria is primary. Dec. 29, when the animal was allowed to drink as desired, there was noted a great polyuria and polydipsia. The dog was killed May 1. Autopsy showed infundibulum widely dilated and gaping. Upon median section small cicatrices of the former lesion seen in the infundibular cavity at the right. At the left the lesion is doubtful. The stalk is intact; the hypophysis is intact. In A solid line indicates urinary output; broken line, water ingestion. B, base of the brain with infundibulum (If.) dilated and altered. C, internal aspect of the right hemisphere with lesion showing at X.

In reality, as the autopsies showed, we injured the base of the brain in both operations—the first time involuntarily, the second time voluntarily.

The duration of this polyuria arising from a lesion of the base of the brain is variable—sometimes fleeting, at other times of a more permanent nature. We have seen it prolonged in one

dog more than 15 days (Attila); while in another it was extremely intense and lasted from the operation of October until May when the animal was killed (Moustachu). In this last dog we noted, for several hours after the puncture, a mild glycosuria, whereas the diabetes remained insipid for seven months. We believe that a diabetes equally marked and lasting has never previously been experimentally produced.

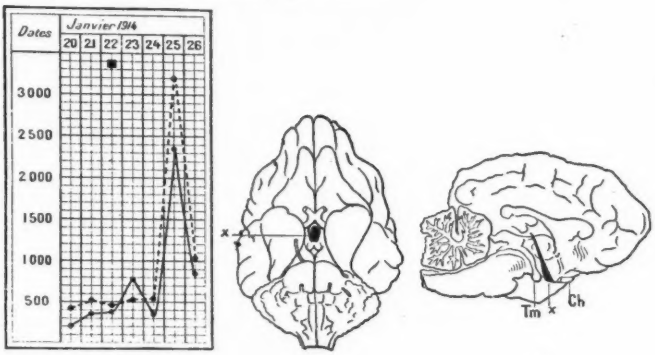

Fig. 4. Male Dog Télémaque (weight 11.7 k.). Puncture of the base of the brain on Jan. 22. Following this a marked elevation of the curve of urinary output is seen, which surpasses the quantity of water ingested (phenomenon identical with that observed in Fig. 3). Animal killed on May 5. Autopsy showed infundibulum gaping and altered. Within the brain substance a symmetrical lesion of the two hemispheres partially traversing the optic thalamus. Hypophysis and stalk intact. In graph A solid line indicates curve of urinary output; broken line, curve of water ingestion. B, lesion of the infundibulum at X. C, lesion X penetrating into the brain and passing between the chiasma (Ch) and the mammillary body (Tm.).

This experimental polyuria was not in the least modified in some animals on which, in the way of tentative therapeutics, we employed injections of pituitary extracts. We tried extracts of the posterior lobe, of the anterior lobe and of the whole gland —H. Carrion & Co. obligingly prepared these for us—and also the pituitrin of Parke, Davis & Co., all with no effect. These results gleaned entirely from our own animals do not confirm those of previous authors.

3. *Site of the cerebral lesions which determine polyuria.* A single glance over the figures we published allows a determination of what is important and what is accessory in the lesions that we produced. A comparative study of these figures, especially in conjunction with the urine charts, quite naturally forces

the conclusions of which we now make a résumé in a few paragraphs.

The lesion which determines polyuria in no way concerns the pituitary body. In five cases in which the experimental puncture has not touched the pituitary body, a consequent in-

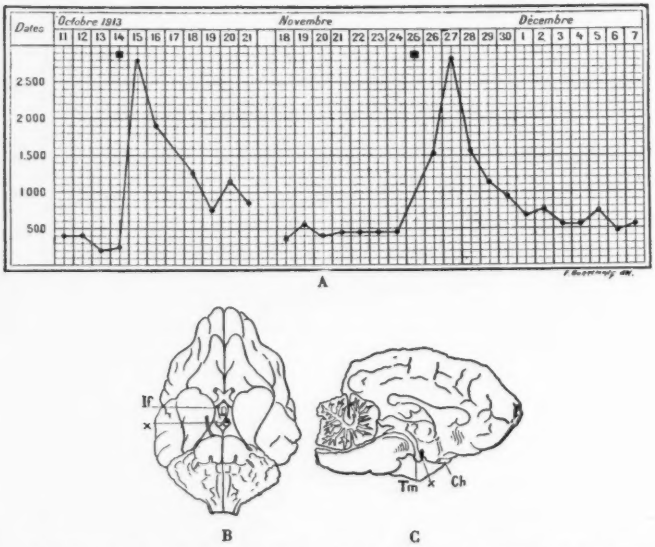

Fig. 5. Male dog Alexandre (weight 1.500 k.). Hypophysis extirpated Oct. 14, 1913, with resulting polyuria, as shown in graph A. On November 25 deep piqûre was followed by a longer lasting polyuria. The autopsy showed: infundibulum slightly dilated; posterior to this a lesion of the left mammillary tubercle independent of the infundibulum; upon median section a superficial lesion of the tuber penetrating 3 mm. and injuring the left mammillary body; in the right hemisphere a similar lesion but less discrete. In the sella turcica there remained a small fragment of the glandular lobe, verified microscopically. The graph A shows the curve of urinary output in the intervening days; B shows the base of the brain with the infundibulum (If.) dilated, and at X the lesion; C, the left hemisphere, showing at X the superficial lesion involving the mammillary tubercle (T.m.).

tense polyuria followed. The polyuria was neither more nor less marked when the pituitary body was involved in the lesion.

The total removal of the pituitary body, done without involving the base of the brain, does not result in polyuria (Agrippine). Nor does a previous ablation of the pituitary body hinder the production of polyuria if, in a second operation, the opto-peduncular region in injured (Alexander and Annibal).

As far as the production and the intensity of the polyuria is concerned, the depth of the puncture and the participation in it of the optic thalamus or of the peduncle seems quite without interest (Amilcar and Télémaque).

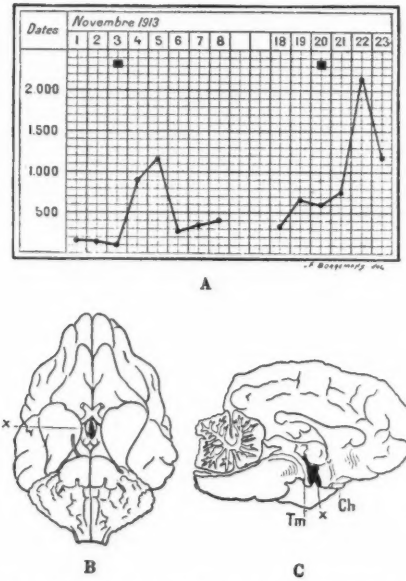

Fig. 6. Male dog Annibal (weight 11 k.). Extirpation of the hypophysis Nov. 3, 1913, followed by polyuria. November 20th deep piqûre was followed by a more marked polyuria. Autopsy revealed the disappearance of the stalk with no hypophyseal tissue in the sella; at the base of the brain the infundibulum gaping and greatly altered; upon median section a gross bilateral lesion extending in depth to the optic thalamus; chiasma intact; mammillary body altered at the left. The graph A shows the curve of urinary output; B, the lesion of the base is here somewhat extended (X); C, in the left hemisphere "X" shows the involvement posteriorly of the mammillary tubercle (T.m.).

The important fact is that a superficial lesion of the base of the brain, often involving only the surface and produced involuntarily in the removal of the pituitary body, is followed by polyuria.

In our animals it seems that the opto-peduncular region alone marks the zone within which a lesion is followed by polyuria. It lies at the level of the grey substance of the *tuber cinereum* in the vicinity of the infundibulum.

A lesion made in front of this zone at the level of the chiasm (Horace), or back of it at the level of the protuberance (Curiace), gives no polyuria.

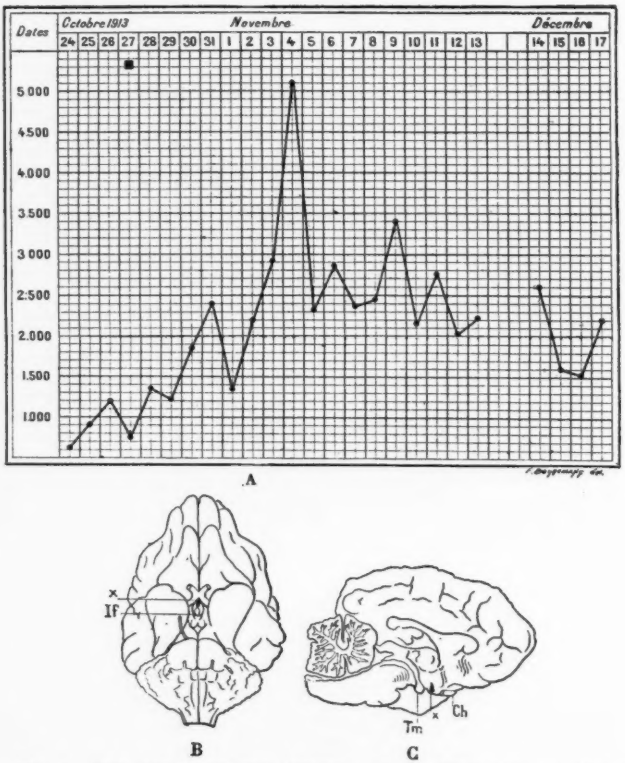

Fig. 7. Male dog Moustachu (weight 13 k.). Piqûre Oct. 27, 1913, and trephining of the sphenoid and penetration thereby of the hypophysis. A considerable degree of polyuria resulted and persisted for several weeks. Autopsy May 17 showed: infundibulum much dilated; anterior to the infundibulum and posterior to the chiasma a light colored nodule forming a projection; hypophysis small and atrophied (weight 0.20 grams); upon median section hemorrhagic linear scar (X) in the infundibular cavity. Graph A shows curve of urinary output; B, the lesion at the base of the brain at X; C, the dilated infundibulum (If.) and the lesion anterior to this at X.

4. *Correlation of polyuria and polydipsia. Regulation of the water retention in the body.* Along with the polyuria we observe, in the operated animals, a marked polydipsia. Is the polyuria primary or only secondary to the polydipsia? To an-

swer this question it is necessary only to put the animal on a constant water régime. That is, after the puncture in the opto-peduncular region we maintain for the animal a constant water intake.

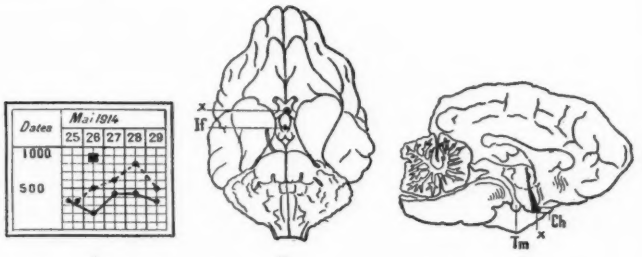

Fig. 8. Male dog Horace (weight 8 k.). A deep lesion made intentionally anterior to the hypophyseal region on May 26, with no polyuria following. Autopsy May 29: Hypophysis and stalk intact; lesion involving anteriorly the chiasma and penetrating to the anterior part of the left optic thalamus on both sides. In the graph A the solid line is the curve of urinary output, and the broken line the curve of water ingestion; B, base of brain showing normal infundibulum (If.) and at X the lesion involving the chiasma; in C lesion (X) is shown penetrating deeply.

This we have done with many dogs and we have seen the polyuria appear with no possibility of an increased water intake for the 24 hours. We even note an increase in the urine volume

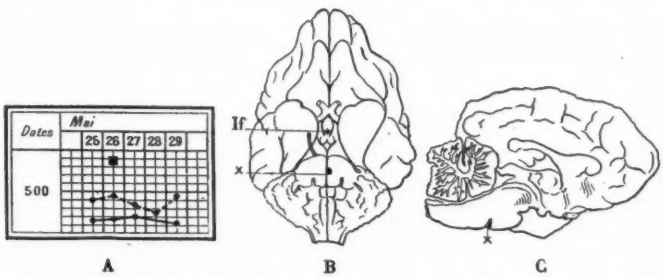

Fig. 9. Male dog Curiace (weight 8.5 k.). May 26 piqûre of the base of the brain made intentionally posterior to the hypophyseal region. No polyuria followed. Autopsy May 29: hypophysis and stalk intact; lesion posteriorly at the middle part of the protuberance and penetrating to the depth of 1 cm. In the graph A the solid line shows the curve of the urinary output, and the broken line the curve of water ingestion; B, the lesion shown at X in the protuberance; C shows superficial lesion at left.

to a point above that of the liquid intake. Under these conditions the water of the tissues diminishes and the phenomenon cannot persist for any length of time without some supplement

in the water given to the animal. If now we offer the animal water as he wishes, he repairs his losses and absorbs an enormous amount of water. Two of the dogs (Amilcar and Télé-

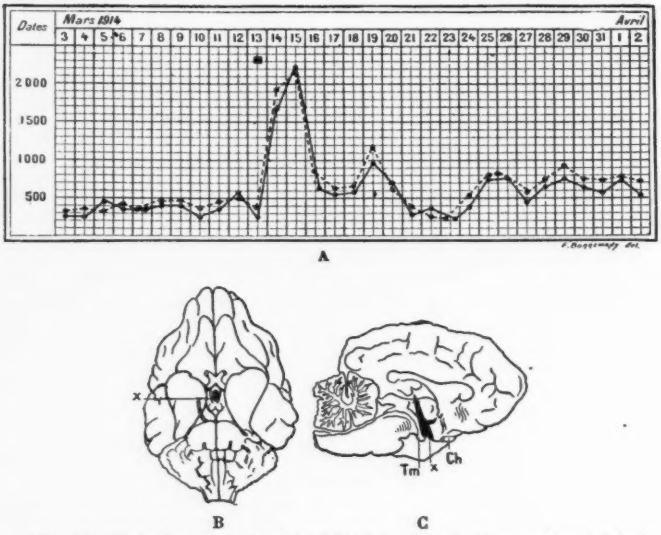

Fig. 10. Male dog Enée (weight 8.500 k.). March 13 experimental lesion in the optopeduncular region, followed by polyuria and considerable polydipsia but equal in degree, indicating no disturbance of water ingestion. The injection of glucose on the 7th and 23rd of March and of caffeine on March 25th gave insignificant result. Urea on the 11th had caused polyuria and on the 18th polydipsia also. Autopsy showed: Infundibulum dilated and altered; within the brain substance a large lesion involving posteriorly the optic thalamus at the left but extending to the right. The stalk is intact and the hypophysis definitely altered. In the graph A the solid line indicates the curve of urinary output and the broken line water ingested; B, lesion (X) of the infundibulum; C, lesion (X) penetrating deeply and involving posteriorly the mammillary body (T.m.).

maque) demonstrate these phenomena clearly—the polyuria following the puncture, then the polydipsia and marked polyuria. These facts allow us to consider that the polyuria is produced independently of the polydipsia.

When all of the animals have all the water they wish to drink, they do not react in identical fashion. Some repair exactly the water losses which the polyuria produces, others repair in excess, while still others repair insufficiently.

The dog Enée repairs her water losses perfectly; with her the regulation of water retention in the body is impeccable.

The dog Castor repairs in exaggerated fashion the losses of water which have been inflicted upon him. It seems that he drinks much more than he has need of, the urine volume being

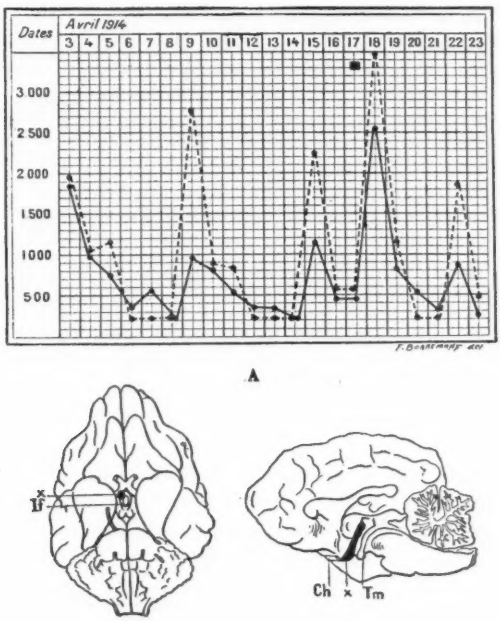

Fig. 11. A young male dog, Castor (weight 12.500 k.). April 17 experimental lesion in the opto-peduncular region, followed by polyuria and considerable polydipsia, but without parallelism, as in the case of Enée (indicating probably a slight disturbance of regulation connected with the youthful age of the animal). The first, second and fourth periods of augmentation of polydipsia were due to previous deprivation of water; the third was secondary to polyuria caused by cerebral piqûre. Piqûre Apr. 17, followed by considerable polyuria. Autopsy showed: infundibulum dilated; lesion anterior and to the right of this latter involving the optic tract; in the depths the large symmetrical lesion, more marked in the right, and reaching to the middle of the optic thalamus; stalk intact; hypophysis intact. In graph A the solid line indicates the output of urine, dotted line water ingested; B, base of the brain with infundibulum (If.) dilated and the lesion anteriorly at X; C, the lesion (X) in the right hemisphere.

secondarily increased. But this dog was still young and it is possible that in him the mechanism regulating the retention of water was functioning in some defective way. It is a classic notion that other mechanisms, other regulators of different func-

tions (circulatory, respiratory, thermic, etc.) comport themselves in imperfect fashion in young animals.

From this group of researches just summarized, there stand out the following conclusions:

(a) It is neither the injury to nor the removal of the pituitary body which leads to polyuria in the dog, but rather a superficial lesion of the base of the brain.

(b) This region corresponds to the opto-peduncular space. In the dog a lesion of this zone is followed by an abundant polyuria. The polyuria thus produced is much more marked and more lasting than that which can be produced in any other way—as by the injection of urea, glucose, caffeine or chloride of sodium or by preliminary water deprivation.

(c) This zone seems to play some part in the mechanism of the regulation of water retention in the organism. Lesions of this region—mayhap in accordance with their extent—are followed by a polyuria either with a parallel polydypsia which means, of course, that there is no trouble with the regulation, or by a polyuria without a consequent polydipsia, which is to say *with* disturbance of the regulator mechanism. Thus as to the production of polyuria we arrive at results sensibly the same as those we obtained in the study of glycosuria and the trophic genital troubles. Many authors have ascribed these phenomena directly to lesions of the pituitary body.

II. HYPOPHYSECTOMY AND GENITAL ATROPHY.

During some experimental researches on the pituitary body we observed, quite as a side issue, trophic troubles of the genital organs.

Our experience was gained from five dogs.

The first dog (Ecureuil), which had suffered a partial removal of the pituitary body, presented neither any modifications in growth, nor any genital atrophy. The second dog (Flick), after total or almost total removal of the pituitary body, has grown enormously—his weight almost doubling—but his genital organs are normal and function normally.

The third dog (Negro), after total or almost total removal of the pituitary body, appears to comport himself normally as far as concerns his development and genital organs.

The fourth dog (Narcisse), after partial removal of the pituitary body and extensive cauterization of the parahypophyseal region, has presented some modifications of the hind quarters and of the extremeties of the limbs with very marked genital atrophy. Obesity did not appear.

Finally in the fifth dog (Moustachu), which did not suffer a removal of the pituitary body but only a deep lesion of the surrounding region, marked polyuria and testicular atrophy developed almost immediately.

Of these five animals only the last two have presented any trophic troubles of the genital apparatus. In the fourth dog (Narcisse) we cauterized the region of the pituitary body and almost certainly we must have injured the neighboring parts since the animal developed difficulty in coördination and equilibration, symptoms which this dog alone, of all the great number we have worked with, showed. In the fifth dog (Moustachu) we purposely made a lesion of the base of the brain.

These experimental facts allow us to conclude that in the incidence of atrophy of the genital organs we are dealing rather less with any hypophyseal lesion than with trouble at some point in the base of the brain, the exact site of which remains yet to be determined with more precise methods.

As far as the obesity is concerned, it seems that it is not necessarily dependent upon the existence of genital atrophy and, moreover, that it is possible to see a breaking up of the "adiposo-genital syndrome." In this regard it is fair to question whether the adiposo-genital syndrome may not be due to lesions of separate centers—often affected coincidentally but not necessarily by the same process.

III. THE GLYCOSURIA OF HYPOPHYSEAL ORIGIN.

Our experimental researches on hypophyseal glycosuria may be separated under two heads: (1) those dealing with a spontaneous glycosuria consecutive to an operation on the pituitary body, and (2) those which deal with the tolerance of the operated animals for carbohydrates.

1. *Glycosuria observed after an operation on the pituitary body and the adjoining part of the base of the brain.* These researches on the glycosuria appearing spontaneously after opera-

tions on the pituitary body and the bordering region, included 45 dogs and 9 cats. In the 45 dogs, glycosuria was observed but 6 times. That is, in 39 cases the result, so far as the presence of sugar in the urine is concerned, has been negative.

We may make further subdivisions in these 39 cases. In 30 of the animals we have not produced any lesions of the base of the brain. In 14 of these 30, the ablation of the pituitary body seemed to us to be entire. It seems useless to discuss here the question of total removal, histologically speaking, and of remnant adherent hypophyseal tissue. At another time we will come back to this point. The only essential matter, as far as the glycosuria is concerned, is a profound blow to the pituitary body and, particularly, the removal of a fair share of the pars nervosa. Thus, we repeat, in 14 of our animals the removal seemed to us to be complete. In the 15 others the removal has been partial—often very considerable—and, for the most part of the cases, especially involving the pars nervosa.

In all these cases, let us repeat, we have not observed any glycosuria after the operation.

In 9 other dogs we have made, voluntarily or involuntarily, a more or less extended lesion of the tuber and of that region of the base of the brain bordering on the pituitary body.

In these 9 cases, 3 times (once partially and twice totally) the pituitary body was removed at the same time that we injured the base of the brain. In the 6 other cases, the base of the brain was wilfully injured, leaving the pituitary body untouched. In these 9 animals we did not observe any glycosuria.

The dogs which furnished these 39 negative cases represent every category. There were adult or aged dogs, dogs but a few weeks old and dogs in gestation. The phenomenon was thus not influenced by the animal's age, sex or physiological state of gestation.

This brings us to the 6 cases in which we have observed positive results. We may subdivide these as follows:

One time we were dealing with the apparently complete removal of the pituitary body in a dog in gestation. This dog has not as yet been killed and we do not know what the state of the brain is.

Twice the brain was manifestly badly injured.

Once we had cauterized the hypophysis and the neighboring cerebral region.

Once we cauterized the hypophysis with a red hot iron and it can scarcely be doubted that the adjoining regions were involved in this energetic procedure.

Once, finally, the removal seemed complete and the autopsy disclosed no lesion of the brain. In this case, however, the glycosuria was inconsequential.

How does the glycosuria show itself in these positive cases?

It appeared rapidly following the operative shock. It was always *light* and *fugacious,* disappearing in from less than 24 to 36 hours after the operation. It appeared quite independently of the polyuria which was often marked even without this glycosuria, as we have cited in numerous cases (Cf. Bull. Société de Biologie). The character of the food consumed prior to the operation seems to have had no influence on the appearance of the glycosuria.

Remember that of the 6 positive results in the 45 operations on dogs, *at least 4* showed lesions of the base of the brain.

In the cat after 4 out of 9 partial ablations of the pituitary body, glycosuria occurred—suddenly appearing and disappearing. Under our experimental conditions the glycosuria seems to be more easily attained in the cat than in the dog, but as yet we are unable to state any fixed rule as to its mode of production.

2. *Tolerance to carbohydrates on the part of animals deprived of the pituitary body—alimentary glycosuria.* We have given glucose, through an oesophageal tube, to some dogs totally or in part deprived of the pituitary body.

We determined the quantity of glucose which just produces glycosuria. Then, administering a slightly smaller amount of the substance, we injected into the animal an extract from the pituitary body (the posterior lobe, the total gland or only the anterior lobe). Thus, if we had found that 90 grams just gave a glycosuria, we administered 80 or 85 grams, injecting at the same time the hypophyseal extract.

Conclusions: a. The different interventions practiced on the pituitary body—partial removals of one or both lobes

or total removal—modify in appreciable fashion neither the tolerance to carbohydrates nor the appearance of alimentary glycosuria.

b. The injections of concentrated extracts of the posterior lobe, the anterior lobe or of the whole hypophysis, do not sensibly modify—in the animals operated on—the limit of tolerance to carbohydrates.

THE RELATION OF THE THYROID AND OF THE ADRENALS TO THE ELECTRIC CONDUCTIVITY OF OTHER TISSUES *

G. W. Crile, M.D., Cleveland, Ohio

The Thyroid—Osterhout has shown that iodin increases the electric conductivity of living vegetable tissue. In our laboratory in a research undertaken in collaboration with Miss

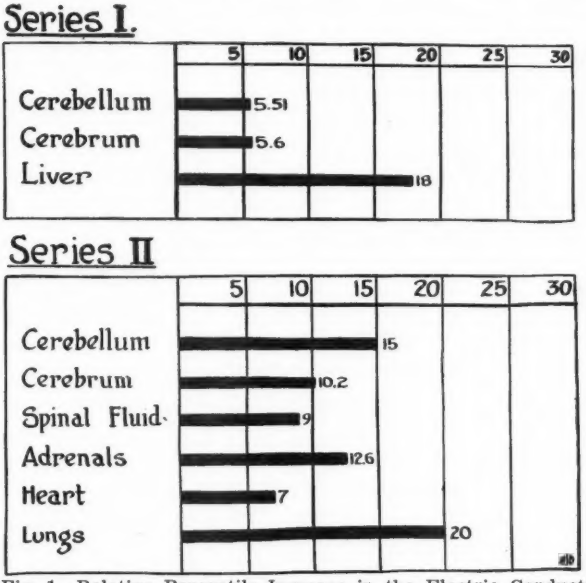

Fig. 1—Relative Percentile Increase in the Electric Conductivity of Various Organs and Tissues Produced by Iodoform averages from two series of observations.

Helen R. Hosmer and Miss Amy F. Rowland, we have found that the electric conductivity of the brain, the liver, the spinal fluid, the heart and the lungs, is increased in iodism produced by the injection of idoform into the peritoneal cavity (Fig. 1). A limited number of observations indicated that an

* Read before the Association for the Study of Internal Secretions, New Orleans, April 26, 1920.

increased conductivity of the brain and the liver is an early effect of thyroid feeding. In exhaustion produced by thyroid feeding for prolonged periods the conductivity of the brain is decreased as in exhaustion from other causes.

The relation of the increased electric conductivity produced by iodin to the function of the thyroid gland becomes apparent when we consider that, as far as is known, the only function of the thyroid gland is to metabolize, to store, and to deliver iodin; and that the excessive administration of iodin will produce symptoms identical with those produced by abnormal amounts of thyreo-iodin manufactured by the thyroid gland. A limited number of observations indicate that excessive iodin and excessive thyroid activity alike produce increased sensitivity to adrenalin, increased metabolism, increased respiration, tachycardia, elevated temperature, with ultimate emaciation, delirium and death.

Iodin is an essential element in the normal functioning of the organism. Iodin is found only in traces in other tissues and organs of the body outside the thyroid. It is the function of the thyroid gland alone and it is the only proven function of the thyroid gland to take in iodin from the blood, to manufacture it into the compound in which it will be of the greatest use to the organism and to give it to the circulation as called for by the needs of the organism.

The normal activities of life in the normal individual are made possible by the amounts of iodin received from the thyroid. Abnormal amounts of iodin increase the activity of the organism as a whole. In the light of our experiments this increase may be interpreted as due, in part if not wholly, to the effect of iodin upon electric conductivity.

Exophthalmic goiter patients tolerate iodin poorly. If too much iodin or thyroid extract be given to a patient with simple goiter, exophthalmic goiter may be induced. Such cases are identical with exophthalmic goiter induced by any other cause.

On the other hand, if the thyroid gland does not metabolize sufficient iodin to meet the need of the organism there results a condition of subnormal metabolism in which the individual is dull, stupid, and more or less in a state of torpor.

The Adrenals—Our electric conductivity researches have shown that a single dose of adrenalin immediately increases the

conductivity of the brain. The administration of an excessive amount of adrenalin causes a decreased electric conductivity of the brain (Fig. 2). This action of adrenalin is probably due to its influence upon oxidation.

The immediate activating effect of adrenalin is most strikingly demonstrated in the reaction to the Goetsch test in cases of exophthalmic goiter.

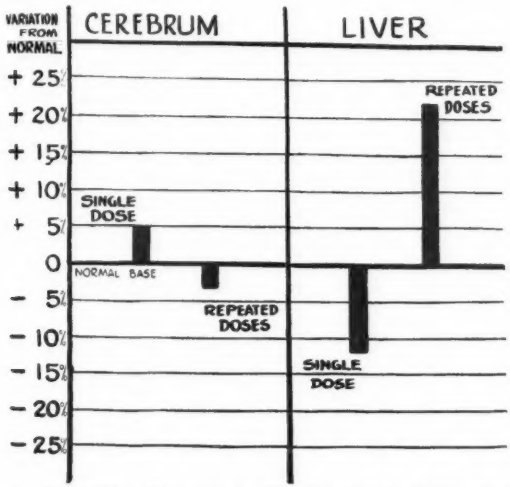

Fig. 2—Percentile Changes in Electric Conductivity Immediately After the Injection of Adrenalin and After Repeated Injections (Note Antithetic Effects on Brain and Liver).

If we accept the view of physicists and bio-chemists—notably DuBois-Reymond, Nernst, Bethe, Lillie, McClendon, Mathews, Osterhout, Loeb, Crehore and Williams, Ostwald, A. V. Hill, etc., that the functions of the cells of the organism relate to electrical processes, it would appear that the fabrication of electric energy within the brain cells is immediately due to oxidation; that oxidation in turn is facilitated by adrenalin; and that the passage of the electricity through the tissues is facilitated by thyreo-iodin.

The interaction of these two agents within the organism may be best demonstrated by a consideration of their relation to exophthalmic goiter .

The Thyroid and the Adrenals in Their Relation to Exophthalmic Goiter—Iodin increases the electric conductance of living tissue; increased electric conductivity is probably synonomous with increased permeability; increased permeability increases function.

According to Ashoff and Cannon stimulation of the nerve supply of the thyroid causes a discharge of thyreo-iodin; hence, we may suppose that the output of iodin is in part, at least, under the control of the nervous system. In exophthalmic goiter there is marked nervous activity, and we may suppose that the thyroid is under active stimulation. That this is the case is shown by the low iodin content of the gland in exophthalmic goiter. According to Cannon and others adrenalin activates the thyroid. We assume that the stimulated thyroid throws out large amounts of activating thyreo-iodin, which by so much facilitates permeability, hence increases activity of the body, including the activity of the thyroid itself and of the adrenals. Oxidation is the basic process in metabolism; adrenalin increases oxidation; iodin increases electric conductance, hence increases metabolism.

Therefore, through the mediation of the nervous system, a reciprocal interaction is established among the thyroid, the adrenals, and the nervous system. Iodin alone, adrenalin alone, thyroid extract alone, emotion, exertion, or infection alone, each causes a "Kinetic Drive" with phenomena similar to those of exophthalmic goiter.

If the foregoing interpretation be correct, then the drive of exophthalmic goiter should be diminished by lessening the activity of any of the three interacting organs—of the brain, by rest cure; of the thyroid, by its resection; of the adrenals, by their partial removal. Although evidence of the positive value of the last-named procedure is thus far incomplete, nothing in surgery is more striking than the immediate benefit of the surgical treatment of exophthalmic goiter.

It is of interest to note that the active principle of the thyroid secretion has been synthetically produced by Kendall; adrenalin is synthetically made and the generation of electric energy is a commonplace; hence, the equivalents of the activators of exophthalmic goiter, of emotion, of exertion, and of fever may be made in the laboratory.

SECONDARY SEXUAL CHARACTERISTICS AND ENDOCRINOLOGY

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INTRODUCTION

The question as to the physiological conditions determining the secondary sexual characteristics has been for twenty years the subject of numerous and important researches. Not only do these characteristics form in themselves an imposing array, morphologic, physiologic and psychic, but it was early discovered that their relations, one to another, are particularly close. From the point of view of general biology the problem perhaps presents a more suggestive aspect: the characters in question which appear at the time of puberty and serve to give the animal its distinctive attributes, male or female, are more or less superadded or supplementary and can, better than any others, be eliminated without endangering the life of the subject. Their evolution and their suppression are quite accessible to scientific investigation; their study promises not only to afford specific data but also to throw a light on the general problem of morphogenesis. If, finally, it is considered that in certain species the secondary sexual characteristics are utilized for the determination of the race, it is seen that the problem, transcending its immediate interest, may lead us to the mechanism of the evolution of species. Such are the ideas which have inspired the present article. It is proposed to discuss the endocrine role of the testes of fowls and the deductions which may be derived.

I. HARMOZONE AND GROWTH

Secondary Sex Characteristics. It will at once be recognized that cocks afford particularly favorable material for such studies. Their secondary characteristics appear in great variety and in adults are easily perceptible grossly. Among such features are the great development of the comb, wattles and auricular appendages which, at puberty acquire a well-known redness; the ruffle of supple, tapering plumes about the neck *(camail)* and across the back *(lancettes);* the long and recurved caudal

plumes, large and small; spurs at the bases of the metatasals; —such are the morphologic criteria.

On the psychic side the array is not less varied: the strongly developed sex impulse leads to ardent regard toward the female and querulous intolerance toward male rivals; by lusty crowing and spirited strutting the emotions are given vent and victories announced.

Since these characteristics appear sharply at the time of puberty,—i. e., with the development of the testes,—biologists have not hesitated to postulate their dependence upon the sex glands. Castration experiments and the necessary control experiments, however, have failed wholly to justify such a generalization. It is true that if the genital glands are extirpated in young cocks the comb and wattles remain small, pale and rather bloodless; neither the amorous nor the combatative instincts appear and our animal maintains a demure silence. But on the other hand the spurs elongate in the absence of the gonads. As we have shown, they grow as rapidly as in the intact animal (1). There is no demonstrable relation between their development and the internal secretion of the male glands. Nor in the matter of plumage have we been able to establish any relation, either in the common variety of fowls which is raised about Paris or the Faverolles and Dorking races. It is true that Morgan, operating upon Seabright cocks (2), obtained an unexpected result,—the development of a magnificent male plumage of which the animals are normally destitute. This is an important fact to which we shall revert. In every case it is possible to recognize an influence of the testes upon only the erectile organs, the sex instinct and the voice. Every control experiment has remarkably verified this point of view. The most decisive, in the opinion of the writer, consists in ovariotomy of pullets, which has been carried out simultaneously by Goodale (3) and by me (4, 5). Deprived of the sex glands the young fowl rather soon undergoes a transformation and acquires the plumage and the spurs of the cock. The metamorphosis is definitive. Hens without ovaries, which have been kept for several years, have with each moult retained the male type of plumage, while their spurs have reached a cumbersome length (9cm.).

That the testes mediate their influence through internal secretion is demonstrated by two sorts of facts: (1) the characteristics abolished by castration reappear if one transplants into the peritoneum thin fragments of testes (Berthold, Foges, Pézard); (2) the same result is obtained by periodical injections of testicular extracts (Loewy, Pézard). We have personally employed in such experiments extracts from the glands of cryptochidic hogs which, it is claimed, are reduced to interstitial tissue only. Since, with several repetitions of the experiment, concordant results have been obtained, we must conclude that the testes elaborate an internal secretion with morphogenic role (harmozone-Gley) and that this harmozone possesses a physiologic specificity.

(*a*) *Law of Continuity.* These preliminaries having been established we reach now the vital part of the subject. In a remarkable report in 1913 Gley (6-p. 57) formulated a problem relative to the internal secretions in which endocrinologists have not failed to become much interested. "If one now considers but a single part of the developmental mechanism (the action of the internal secretion on development) it can be no better explained than by the idea that this development is arrested of itself at a given moment. Is it to be supposed that the interstitial tissue of the testicle—or similarly, any other organ, diminishes its functioning, reduces, for example, the amount of active substance which it sends to the organs on which it works? *But there is no proof that such functional diminution occurs,* and, moreover, these substances act in very minute doses, hence it is the absolute suppression of their functioning that would have to be supposed. The problem is pending."

Our experiments in post-pubertal castration allow the settling of the debate and the demonstration of the judiciousness of the reservations formulated by Gley.

If it is a fact that the endocrine function of the testicle stops at the moment when the secondary sexual characteristics, which are conditioned by its activity, have reached their complete development, the extirpation of the genital glands ought to be from this time on without effect on the animal.

Now that is not what occurs. If we castrate an adult cock at full sexual maturity, a few days later the sexual instinct and

the crowing definitely disappear. The erectile organs begin an immediate regression: they diminish in volume, grow pale, and finally acquire the reduced dimensions of the homologous organs of castrates. From the periodical measurements of the comb we have determined that the regression occurs with remarkable regularity, though this does not mean that the rapidity is constant. On the other hand, sections made of the erectile tissue show that the structure of this tissue has not been visibly affected, therefore the phenomenon should be imputed to a real regression.

We have carried out our experiments on cocks of different ages and have obtained the same results. Always, the regression of the comb is effected according to the same rhythm, going from the initial constant stage (sexual comb) to the final equally constant stage (capon's comb).

All these facts show clearly that the testicular function is constantly necessary for the maintenance of the erectile organs and the sexual instinct. Gley reasons correctly when he states that there is no proof of functional diminution. We can even say, in view of the uniformity of the results, that the testicular harmozone exercises a *sustaining action that is always equal.* It is true that the duration of the experimental regression of the comb is slightly increased with age, but we are tempted to see the explanation for this, not in the harmozone itself, but in a conditional property of the tissue.

We can further affirm that the internal secretion of the testicle disappears immediately after castration; that is to say, it does not outlast the ablation of the genital glands,—its action is *immediate.*

This was indicated by the manner of the beginning of the regression. We will state forthwith that all harmozonal persistence, after castration, would have as its result a more or less continued persistence of the characters it influences. Now what do we find? The regression of the comb immediately follows castration: the regression is maximum for the first few days at its beginning, a fact which is shown on the charts by a sharp fall in the curve. Thereafter the regression is retarded and, finally, the curve becomes horizontal. The regression is then at an end. Now the sharpness of the decline as established for

the beginning of the phenomenon is incompatible with the persistence of the harmozone. It must then be admitted that the harmozone is effectually destroyed in the blood. Moreover, we have established that for the injections of testicular extract to be efficacious they must be repeated very often, which indicates still further, a rapid destruction of the active product.

I conclude: The continuity of the endocrine function of the testicle is an indispensable condition for the maintenance of the conditioned characters. The morphogenic action of the testicle presents in addition a remarkable constancy which is dissembled by the arrest of growth in the adult.

It may be remarked in passing that the acquisition of these suggestive ideas is the consequence of two particularly favorable experimental conditions in our studies: on the one hand the possibility of measuring the comb, which permits a continuous cinematic study, and on the other hand the reversibility in the growth of that organ which makes significant the counter-proofs.

(b) Law of Minimum Efficacy. Observation shows that the glands of internal secretion are more than sufficient to assure the role that has devolved upon them. All biologists know that an insignificant fragment of the adrenal or thyroid preserves the animal from the consequences resulting from the complete extirpation of these glands. There is a luxus endocrine secretion, as there are digestive secretions in excess, as there is a margin of safety in respiration (6-p. 50). Is this so in the case of the testicle?

Two types of facts permit an affirmative answer: the frequently unsuccessful attempts at castration of cocks and the systematic experiments in testicular transplants. Minute fragments of testicles scattered in the peritoneum, far from the normal locus of the gland suffice to activate the development of true male characters and to assure their maintenance: such is the usual result.

In view of this effect, we have attempted to determine the mass of testicular substance below which the tissue is incapable of exerting its function. But apropos this subject a preliminary remark is necessary concerning the structure of the testicular nodules. These structures are highly variable and we classify them into three categories: (a) nodules having con-

served, even a year after castration, the normal aspect of the cock's testicle, seminal canals containing spermatids with almost no interstitial tissue; (b) nodules presenting the seminal canals degenerated and reduced to a few Sertolian nuclei scattered in an extremely vacuolated cytoplasm with interstitial tissue more abundant; (c) completely necrosed nodules, comprising degenerated seminal canals replaced by connective tissue in which interstitial cells are rare. The first two types alone are efficacious and it is with them alone that one can make weight comparisons.

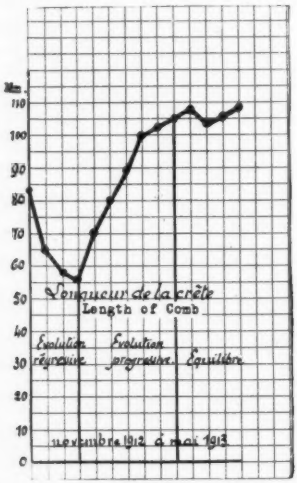

Fig. 1. Graph showing the changes in the length of the comb of a cock succeeding castration. A regressive stage is followed by a progressive stage and final equilibrium.

On the other hand an elementary precaution is imposed relative to the appreciation of the secondary sexual characteristics of a subject. *An isolated observation means nothing.* In order to judge of the state of these characters, a long continued cinematic study is necessary. For example, in fig. 1 are presented the data regarding a cock which we had castrated in November, 1912 and which had received at the same time some ovarian fragments from a hen. For a month the comb diminished, going from 84 mm. to 56 mm.; then suddenly the growth of the comb again commenced and from December to April the length increased

from 56 mm. to 108 mm. At autopsy we found a testicular nodule weighing 1.5 gm. An isolated observation would have made us consider the animal in December a castrate, in February an incomplete castrate, and in May a normal animal. So the characters should not be appraised until they have attained an equilibrium.

Neglecting this precaution, Foges (7), in a memoir relative to testicular transplantations in cocks, has reported results the interpretation of which is open to question. During the course of his study, carried out on 33 animals, he made but a single measurement the data of which, according to our mind, lead to a false conclusion. The data may be quoted:

	Comb		Wattles		Spurs
	Height	Base	Height	Base	Length
Control-cock	8	12	5½	2	2
Capon No. 1.....	4	8	2½	2	½

From this Foges concludes that in cock No. 1, which possessed two testicular nodules, the growth of the comb, wattles, and spurs, is diminished. And yet he has earlier admitted that in capons "the spurs can exist just as in the hens." In reality, animal No. 1 is probably a castrate the spurs of which have developed tardily.

Having made these reservations with regard to methods, we will again turn to the question of the transplant-bearing cock. In subjects presenting *characters in equilibrium* and with *functionating nodules,* we determine at autopsy the total mass of the fragments. We have found that these subjects can be divided into two groups: those that possess more than 0.5 gm. of testicular substance have the aspect of normal males; those that have less than 0.5 gm. are essentially castrates. The mean weight of the testicles being 15 gm. it is evident that the endocrine function of the testicle is assured when 1/30 of the normal gland weight is present. *The testicle does not deviate from the law of luxus secretion.*

(c) *All-or-none Law.* We are naturally led to an examination of the correlation that may exist between the mass of testicular parenchyma and the quantitative development of the conditioned characters, a correlation that is particularly interesting as we approach the minimal effective limit. If we consider the figures relative to those of our subjects the characters of which were in equilibrium, and to make the matter more clear, if we

arrange them in the order of diminishing size of the testicle and compare the weight of the seminal parenchyma in grams with the length of the comb in millimeters, we can establish a curve as shown in figure 2. The ordinates correspond to the succession of animals as in the table and the abcissae to the weight of the testes and length of the comb.

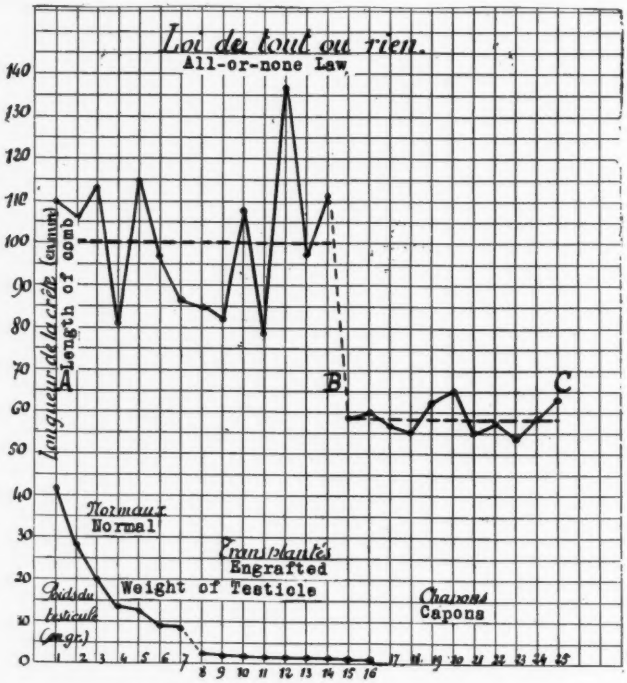

Fig. 2. Graph showing the length of comb as related to the weight of testicular tissue present in 25 cocks.

No.	Wt. Test.	L. Comb	No.	Wt. Test.	L. Comb	No.	Wt. Test.	L. Comb
1	42	110	9	1.5	82	17	0	56
2	28	106	10	1.5	40	18	0	55
3	20	113	11	1.0	78	19	0	62
4	14	81	12	1.0	137	20	0	65
5	12.5	115	13	0.7	97	21	0	55
6	9	97	14	0.5	111	22	0	57
7	8.3	86	15	0.1	59	23	0	54
8	2	85	16	0.1	60	24	0	58
						25	0	63

An examination of the chart shows clearly that there is no parallelism between the testicular weight and length of comb. In the part A-B of the curve which pertains to the cocks showing male characteristics, the curve is very high and presents variations; but these vary from one side to the other with a mean value of 100; they do not correspond to the variations of the morphogenic power of the testicles, but to racial characteristics, and are the result of the fact that the cocks to which they pertain are of different races. The part B-C of the curve which corresponds to the so-called neutral cocks, also shows variability but relatively less marked. Without doubt the variability again is to be ascribed to difference of races. The subjects fall in series with those of the region A-B and consequently are comparable with them; the mean of the second part of the tracing is 58.

At the point B the least efficacy is found; the curve here undergoes a sudden drop, passing from the level A-B to the level B-C. This turn of the curve and its obvious *discontinuity* seem to us, better than any reasoning, to show that the morphogenic effect of the testicle follows an *all-or-none law.* That is to say, *as soon as the functional threshold value is passed, whatever may be the mass of the active gland, a cock takes on as a whole its secondary sexual characteristics.* It appears that these manifestations can not be fractionated.

It would be interesting to determine if the moment these characters are started in their development in the cock is exactly that point when the testicle has attained this minimal weight of 0.5 gm. In this case the morphogenic action of the testicle would be at the beginning and throughout the sexual life a constant which directs the conditioned processes. There would result a great simplification in the study of the growth of the comb. Further researches should decide the question.

The all-or-none law carries another implication of general significance in relation to the factors operative in all conditioned growth. When one studies the morphology of the testicle of a cock, a uniformity of structure is found throughout the whole extent of the gland; moreover, this is maintained throughout the first years of life, from the third month on. Since the testicle is richly vascular, the conclusion is justified that the amount of the active harmozone thrown into the blood is proportional to the

amount of active parenchyma,—that is to say, in short, to the total weight of the gland (with the exception of the albuginous matter). If this harmozone actually constituted merely a substance promoting unrestricted growth, there is no reason to believe that the law of mass action would not obtain. The two curves in figure 2 would have the same trend, which is not the case. The observations cannot be interpreted unless one admits on the part of the harmozone a *stimulative action* upon a tissue the growth capacity of which is limited. This growth capacity which is a property of the conditioned organ represents, in these circumstances, the influential factor.

HARMOZONE AND EVOLUTION

(*a*) *The Sebright Breed.* In 1918 we wrote: "The theories of evolution presuppose the occurrence of progressive organic modifications which effect the transformation of the animal species through growth or atrophy of the organs. The environmental influence, the manner of living, the habits, constitute, outside of sexual reproduction, the possible causes of individual variations. One may well ask if the action of these different factors has no influence on the harmozones, the directors of the morphogenic processes. In fact an equilibrium can not be modified if something has not disturbed the cause operative in its maintenance; on the other hand, every cause acting on an endocrine gland is profoundly echoed throughout the entire organism."

This point of view has received confirmation through two observations as exact as they were unexpected. The first is related to the Sebright cocks, so well studied by Morgan.

Considered as very close to the original ancestral strain of the *Gallus domesticus* the Sebright variety differs from ordinary cocks by the racial characters selected from the secondary sexual attributes; they have neither hoods nor lancets; the recurved plumes hardly extend beyond the straight feathers of the tail. In fact so lacking are they in these male attributes that their plumage resembles more that of a hen. The wattles and the comb, however, are always of the characteristic male type. Now it is a curious thing that if a Sebright cock is castrated, there develops a rich male plumage, as has been shown by Morgan; hoods, lancets, and the curved caudal plumes elongate measureably; the animal loses its racial peculiarities and follows the

common law. It should be noted that in this circumstance the testicle, far from conditioning the male plumage, as has been previously considered, seems, on the contrary, to exert an inhibiting action similar to that of the ovary.

In the absence of histological studies of the testicles of the Sebright cock, in order to explain the plumage characters, we have thought of a state of false equilibrium, a condition which would be supplanted by castration or by a violent traumatism (1-p. 143). New studies advanced by Boring and Morgan (8) prevent us from attributing the cause of the anomaly to a somatic property of the cocks, and oblige anew a return to the conception of a conditioning by harmozone activity. In fact, on examining the structure of the testicles of the Sebright cocks, Boring and Morgan found a special type of cell which is not found in the testicles of other cocks. They are large elements with well defined margins, clear cytoplasm, nucleus more or less spherical, and forming more or less well defined islets in the interstitial tissue. Near them masses of yellow pigment were observed which suggested for the elements in question the name of lutein cells. Now the lutein cells are a normal part of the ovary of the hen (Boring and Pearl) ; we have described similar structures in the ovaries of the silver pheasant, *Euplocomus nycthemerus* (1-p. 116). Since these interstitial cells in the female ovary prevent the development of the male plumage, we believe with Morgan that the same is the case with the Sebright cocks. This now explains the assumption of the male plumage after castration.

It is certain that the special characters of the plumage of the Sebright cocks give to these animals an apearance such that one would think they are of a different species. These racial attributes strike the most casual observer much more than the histological structure of the gland. However, if one establishes a subordination of characters, as results from our studies on conditioning, one should admit that the presence of lutein cells is a dominating character, while the specialities of plumage constitute a subordinate character. From this, we must conclude that if, in the evolution of the *Gallus domesticus*, a *variation is produced at a given moment*, with regard to the plumage *it has been preceded, prepared, unloosed, by a correlative modification of the conditioned glands;* our hypothesis receives verification in an exact manner.

The zoologists ask a question here that can not be allowed to pass. Which is the primitive form, the structure of the testicles of the Sebright cocks, or the ordinary structure? It is customary to consider the Sebright cocks as being the older strain, on account of the simplicity of their plumage and because of their resemblance to the cocks of Asia. The conditions of breeding and selection have brought about the development of races having most luxurious male plumage, such as those of Japan, in which the tail has taken on an extraordinary development; this seems clear.

But the conclusions are reversed if one considers that castration causes the appearance in the Sebright cocks of the abundant plumage of the males. These animals possess then *in a potential state,* the same characters as other cocks, and an *added influence* has been necessary to prevent the development of these characters at puberty. From that point of view one should consider them as being more highly evolved. This notion of potentiality deserves to be retained when it is a matter of comparing racial characteristics; it forces us to revise our judgments based on simple morphological ideas. What problems still remain to be studied!

The Sebright cocks are not unique in the possession of simple plumage. According to Morgan and Boring, one finds in the Campine and Hamburg races cocks having plumage like that of a hen. In these species it is simply a matter of exceptional cases,—the majority of the males having normal plumage. Without doubt, no histological study has bound up these accidental variations with the structure of the genital glands, but it is allowable, in view of facts already acquired, to prophesy an accidental variation in the structure of the male glands. We would witness, if that view is correct, an actual transformation in the plumage equilibrium, a change brought about by a preliminary transformation of the conditioned gland. Intensive studies alone can definitely decide the question.

(b) The results of exclusive carnivorous diet in cocks and rats. One such mechanism is assumed in the supposition that the reproductive glands may be modified by the habitual causes of variation, alimentary regime, state of environment, etc. The time has come to examine the foundation of this allegation.

In a series of experiments carried on from 1901 to 1906, Houssay (9) studied the modifications produced in Gallinacea (cocks and hens) by an exclusive meat diet. Among the results obtained, the author noticed a reduction in the sexual dimorphism: progressive sterilzation, the cocks losing the fighting instinct, etc. Put in the presence of their rivals, certain meat-fed cocks appeared timorous and tried to hide; they did not resist, they were the attacked. More often, they were accepted by their normal companions who did not deign to pick a quarrel with them. We should add for the sake of completeness that the carnivorous régime did not produce constant results and that many cocks on this diet retained the aspect and functions of the normal bird. In all cases Houssay attributes the effect to a direct influence of the meat diet.

Pursuing the same line of thought, Paul (10) submitted several series of male rats successively to an exclusive meat diet. As controls, at the beginning of this regime he took rats that had just been weaned and castrated them; at autopsy he determined that the reproductive organs were little developed in comparison with those of the controls. The reduction affected the seminal vesicles, prostate and penis. Paul attributed the modification to a direct influence of the exclusive meat diet.

In the two cases it is interesting to call attention to the development of the testicles in the animals so modified. As far as the carnivorous cocks are concerned, we have determined, from the autopsy tables accompanying Houssay's memoir, that these glands had received a setback under the meat régime and had not developed,—at least in the animals having the castrate characters. The mass of glandular parenchyma in these various subjects varied from 0.7 to 0.2 gms. Among the meat-fed cocks which retained their sexual attributes completely, the figures are higher, varying from 1.9 to 42. gms. We call to mind here our conclusion relative to the potency threshold and the all-or-none law. A similar conclusion follows from the work of Paul, which is illustrated by two charts showing the reduction of the genital tract and the testicles; the male glands of the subjects submitted to the carnivorous diet are so small in comparison with those of the normal males that one would think them atrophied.

In one case as in the other, it is not expedient actually to attribute the non-development of these secondary sexual char-

acteristics to the direct action of the dietary regime. The truth is that the exclusive meat diet determines in the two species a slow intoxication, an abnormal chemical process, to which the genital glands are particularly sensitive; it has then produced the modifications *secondarily* consecutive to castration. These experiments prove, in our opinion, that the reproductive glands are capable of responding to a definitive chemical influence, even though the nature of the response is not such as to produce a new race.

In conclusion, the testicular harmozone holds as dependents a certain number of secondary sexual characters. Its action, which begins at puberty, presents during the sexual life, in the case of cocks, a *continuity* and a *constancy* that are really remarkable. It does not survive the ablation of the genital glands although a small amount of the glandular parenchyma suffices to assure the integrity of the function. Histological modifications of the gland are able, as in the Sebright cock, to induce modifications in the external characters and to determine the very different races. Finally, these glands are sensitive to the action of a dietary regime considered up to now as one of the primary factors in evolution.

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THE ORIGIN AND EVOLUTION OF THE INTERSTITIAL CELLS AND OF THE OVARY AND THE SIGNIFICANCE OF THE DIFFERENT INTERNAL SECRETIONS OF THE OVARY

Isaac Ochoterena and Eliseo Ramirez, Mexico

In the ovary two functions may be distinguished, one in relation to reproduction and consisting of the development of ova and the other referring to its role as an organ of internal secretions. From this point of view two sorts of histological structures are to be distinguished, the corpus luteum and the interstitial cells.

The corpus luteum was first recognized by Coiter in 1573, and the interstitial cells by Pflüger in 1863. Following Fränkel the reports upon the endocrine function of the corpus luteum have been almost innumerable. The functions of the interstitial tissue have been considered by Limon, Bouin, Fränkel, Regaud, Ganfini, Ancel and Bouin, Below, Graves and Felner.

According to our embryological researches, the corpus luteum has a dual origin from the connective and the epithelial tissue, this being the source of the theca and the membrana granulosa, respectively, from which the corpus luteum is derived. According to Sobotta and Cohn it is of epithelial origin and according to Guilera Molas it is of connective tissue origin exclusively.

Della Drips, who has studied the corpus luteum of the Spermophile, Citellus tridecemlineatus has noted that immediately after the formation of the corpus luteum there appear globules of protoplasmic secretion; these are colored red with the fuchsin-methyl green stain following fixation in Bensley's fluid. This latter is substituted by another secretion of lipoid nature; the latter is related to the post-partum retrogressive changes of the uterus.

In our preparations of the ovaries of rabbits and rats the red elements begin to appear as early as the membrana granulosa and discus proligerous stages of development. The secretory

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activity is manifested, therefore, before the production of the corpus luteum proper (Fig. 1). Our work shows also that the corpus luteum persists until after parturition.

We do not coincide in the opinion of Edem and Lokyer, Fränkel, Asher, etc., that the corpus luteum gives rise to menstruation. In short, the corpus luteum succeeds the rutting period, as demonstrated by us in the rabbit, by Della Drips,

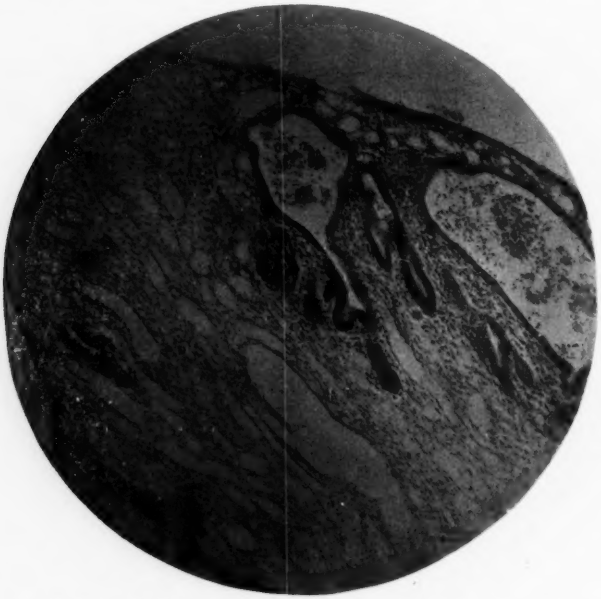

Fig. 2—Microphotograph of the uterus of the rabbit during the rutting period, showing the characteristic modifications of the mucosa, the extravasation of blood and the blood-filled lacunae.

Donaldson and others in different animals; rutting is accompanied by phenomena analogous to menstruation. The accompanying microphotograph (Fig. 2) shows the details observable in the uterus of the rabbit during the rutting. Our work thus confirms that of Wallich. That the sanguineous discharge is to the exterior in women and the macaca is due principally to the anatomical circumstances of the presence of the type of muscular wall found in these primates.

During menstruation arterial hypertension frequently is seen whereas extract of corpus luteum produces hypotension. Such extract, futhermore, is of no utility in the treatment of precocious menopause and does not augment the menstrual flow. In cases of various women, we have noted, on the contrary, a diminution and retardation of the flow, confirming the observation of Epley, MacCann, Climenko and others. We accept as indubi-

Fig. 3—Microphotograph of the cortical region of the rabbit ovary, showing an ovule developing and the interstitial cells, some with two nuclei and one in regression.

table that the secretion of the corpus luteum depresses menstruation, not by inhibiting any hormone secreted by the uterus but by its antagonistic action on the interstitial tissue of the ovary. We have studied the uterus in a great number of mammals and have never encountered any histological formation nor cytological process which would support the existence of a "myometrial gland" nor any definite evidence of internal secretion. We, therefore, take issue with Seitz and Wintz. That bilateral

ovarian extirpation suppresses menstruation is to be ascribed not to loss of corpus luteum but of the secretion of the interstitial tissue.

We have made studies of the interstitial cells, their embryology, evolution and endocrine function, arriving at the following conclusions: These cells may be considered as a constant formation in the ovaries of a great number of animals. The

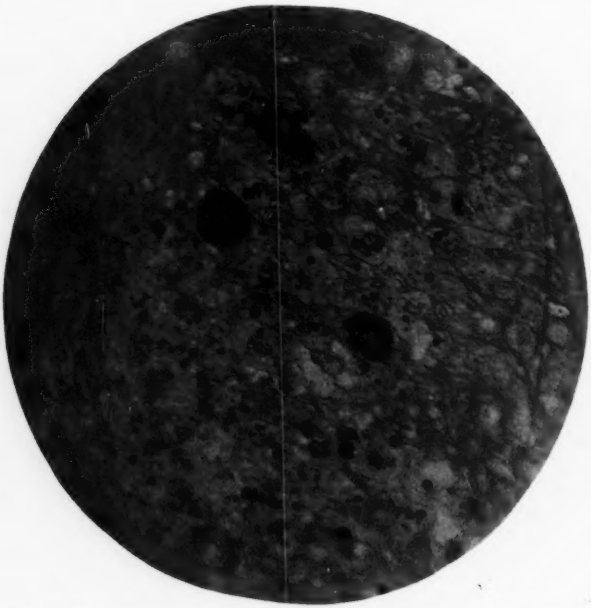

Fig. 4—Microphotograph which shows the interstitial cells of the rabbit ovary. The chondrioplasts secrete lipoid material colored brown with osmic acid.

epithelial cells of the gonads which form a layer in immediate relation with the celom, multiply, invade the subjacent connective tissue, pass through the stages designated by Winewarter the "protobroca" and "deutobroca" and evolve in this manner: some pass through the well known stages to form oöcytes; others constitute the interstitial cellules. These undergo a process of phagocytosis encountered by us in the ovaries of the rabbit (Fig. 3) comparable to that described by the bota-

nists in the sexual elements and by Balfour and Lane-Claypon in other animals. Some of the cells are able to reach a stage analogous to that which precedes the formation of oöcytes, in the cells previously described.

The interstitial cells are the site of a cyclical phenomenon manifested principally by the evolution of chondriosomes. The mitochondria of these cells in which the hormones are elaborated

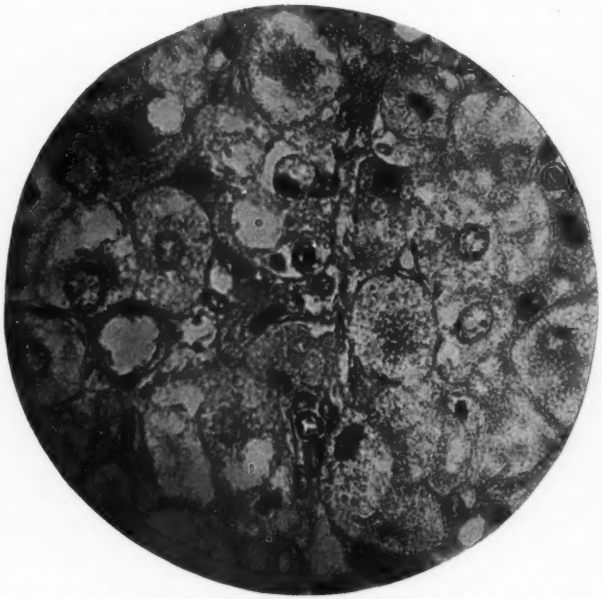

Fig. 5—Microphotograph showing the interstitial cells of the ovary during the dispersal of the chondriomites.

appear in the ovary of the fetus and undergo notable changes during the development of the animal. They are probably concerned in the appearance and conservation of the secondary sexual characteristics and especially the modifications characterizing puberty.

During menstruation in women, and in rutting, which is the equivalent of menstruation in animals, the activity of the mitochondria is clearly evident, characterized by the appearance of chondrioplasts, which in turn give rise to a substance

of lipoid nature that by osmic acid is stained a coffee brown (Fig. 4). At the termination of the rutting period the chondrioplasts give way to the smaller mitochondria and these form the starting point for a new secretory cycle (Fig. 5).

Of the two endocrine functions of the ovary, the corpus luteum mediates that having to do with the formation of decidual cells and the modification of the uterine mucosa which favor nidification of the ovum. If fecundation occurs the structure is transformed to the corpus luteum of pregnancy and alters the nature of its secretion. It assumes relations with the mammary glands and other endocrine organs. The secretion of the corpus luteum being, as previously mentioned, antagonistic to that of the interstitial ovarian cells, when the corpus luteum retrogresses or is experimentally suppressed, the action of the interstitial secretion is manifested. This secretion is the determining factor of menstruation; during the menstrual period the corpus luteum is either non-existent or in a regressive phase, while the interstitial cells manifest with maximum intensity the secretory phenomena. The ovarian congestion which coexists with menstruation favors the maturation of the graafian follicle. This ruptures and gives rise to a new corpus luteum which in turn depresses the interstitial secretion, causes the discontinuance of menstruation and thus again initiates the cycle previously described.

Fig. 1—Microphotograph of a preparation of the ovary of a rabbit. The chondriomites of the zona granulosa have been colored red directly from the slide by aid of the camera lucida. Fixation and staining by the methods of Bensley and Cowdry.

THE INTERNAL SECRETION OF THE TESTIS

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The researches of Mantegazza and Brown Séquard in the second half of the last century on the testis in order to determine if that gland produces an internal secretion which gives secondary characters to the male, opened the way for the study of the endocrine glands.

Although we know, if only imperfectly, the internal secretion of some of the ductless glands and we are able in certain cases, when the function is disturbed, to give treatment with success, the knowledge of the function of the sexual glands, although the first studied, is not even yet well known. This is due to the fact that though the anatomic and pathologic researches of Ancel and Bouin are arguments for the conception that the testis has an internal secretion, which is elaborated from the interstitial cells, the experiment did not give definite proofs.

Ancel and Bouin, after ligature and resection of the ductus deferens in the rabbit, obtained degeneration and atrophy of the seminal epithelium; the Leydig's cells remained without change. The animal kept the secondary sexual characteristics until the day that it was killed. Gosselin, Fabris and others, on the contrary, did not observe lesion of the testis from ligature and resection of the ductus deferens. Hence the conclusion as regards the internal secretion of the interstitial cells of the testis is not uncertain; the difficulty of solution of the problem is due to the disposition of the interstitial cells, which, as remarked lately by Cushing "is such as to make it impossible to observe the consequences of their ablation apart from the other cells of the organ."

Therefore, I believed it would be of value to repeat the study of the internal secretion of the testis and began the investigation herein described. The experiment of Ancel and Bouin was repeated, but with the rooster instead of the rabbit as the experimental animal. The rooster differs from rabbits in that it

has very marked secondary sexual characteristics: the comb, the spurs, the plumage, the sex instincts, the crowing and fighting tendency. After castration these characteristics disappear or become greatly modified. It is indeed easy to distinguish a capon (castrated rooster) from a rooster. If some time following the operation of ligature and resection of the ductus deferens the rooster, while alive, keeps all the secondary sexual characteristics of the male but the testes have become small and, on microscopic examination, atrophy of the cells of the seminiferous tubules is noted while the interstitial cells of Leydig show no lesion, one would be justified in agreeing with Ancel and Bouin that the interstitial cells have the function of internal secretion of the testis.

In addition to simple ligation of the ductus deferens a further experiment was made. Three or four months after the initial ligation, when atrophy of the cells of the seminiferous tubules had occurred, the testes were removed by a second operation. This amounted in effect to extirpation of the Leydig cells. Any changes in the secondary sex characteristics could then be ascribed to loss of these cells.

Fichera has found that castration in the rooster and in other animals produces hypertrophy of the pituitary body with increase of the eosinophile cells. Accordingly, in each experiment the condition of the hypophysis cerebri was observed. In the light of Fichera's results it would be expected that the pituitary body would remain normal after the first operation (ligature and resection of the ductus deferens with subsequent atrophy of the seminiferous tubules) and after the second operation (removal of the atrophic testis) it would become like that of the capon. Control observations were made upon normal roosters and ordinary capons.

Finally the experiment of Pézard and Lespinasse (the transplantation of testicular substance into the peritoneal cavity) was repeated in order to study the eventual change of the secondary sexual characteristic in comparison with the changes of the cells of the testis. In these experiments, also, the pituitary body of each rooster was examined.

The experimental series included many animals, because sometimes we observed reconstruction of the ductus deferens

after ligature and resection. In order to hinder this reconstruction as much as possible the vas deferens was dissected from the ureter for about 2 cm. and ligated at both extremities; at a point midway between the two ligatures a third knot was tied. The vas was then cut between the middle knot and that nearest the cloaca.

Fig. 1—Normal testis of cock. Note seminiferous tubules full of spermatozoa. The spaces limited between two or three seminiferous tubules show the interstitial cells. Fixation, formalin; staining, haematoxylin-eosin; magnification, 60 diameters.

The tissue of testes and pituitary bodies for the histological study were fixed in formalin solution, in Zenker's, in Müller's or in Flemming's fluid; the sections were stained with haematoxylin-eosin, haematoxylin-Van Gieson, safranin-Flemming's, "thionine pheniquée" of Nicolle, and fuchsin of Altmann. Especial regard was paid to degenerative changes and chondriosomes as indicative of secretory activity.

A. THE INTERSTITIAL CELLS OF THE TESTIS OF NORMAL ROOSTERS

This series comprised 7 normal cocks. The testis in the rooster lies in antero-superior part of the peritoneal cavity in relation with the anterior-inferior surface of the kidney. It is an ovoid body of very large size considering the size of the animal; the average weight of the testis in a rooster of about 2½ Kg. is 10 grams. The spermatic ducts are two tortuous canals which extend from the epididymis to the cloaca, where they end. The vas deferens with its nerves and blood vessels follows the internal side of the ureter, and these structures cross the abdomen longitudinally.

The testis is made up of the seminiferous tubules and interstitial connective tissue. The interlobular or interstitial stroma contains groups of peculiar rounded polygonal elements, the interstitial cells. These are more frequent in the spaces limited between two or three seminiferous tubules, where there often is a small blood vessel. The interstitial cells sometimes do not show well defined limits. The nucleus has a spherical form and stains well. Some authors have studied the substances secreted from the testis, particularly the lipoids and pigments (Loisel, Pézard). Loisel says that the cells which lie in spaces between seminiferous tubules of the rooster secrete two kinds of pigments: "les unes, élaborent des pigments clairs, proviennent de l'ébauche germinale et doivent etre considérées comme des éléments soeurs de cellules germinatives; les autres élaborent des pigments foncés, insolubles, sont des éléments conjonctifs hypertrophiés apparaissant à une époque plus ou moins avancée de l'evolution du testicule. Il foudra donc sans doute reserver l'expression classique de cellules interstitielles pour désigner les éléments de la première categorie." I believe that one should consider the fat and especially the chondriosomes of the interstitial cells, because they give evidence as to whether the cells have secretory properties. The detection of the pigment in cells, when we are able to establish that they elaborate these pigments, does not demonstrate that the cells have a secretion.

I found in the interstitial cells of the testis of the rooster small and numerous fatty granules (safranin-Flemming method) and many small granules (mitochondria) well stained by the acid fuchsin with Altmann's methods. Rasmussen also found

mitochondria in the interstitial cells of the testis of the woodchuck.

B. THE PITUITARY BODY OF NORMAL ROOSTER AND CAPON

The pituitary body of the rooster (Piersol) consists of two distinct parts, the anterior and posterior lobes. The anterior part (glandular) constitutes the major part of the organ. It is surrounded by a fibrous capsule that is continuous with the thinner one inclosing the posterior lobe. We shall first consider the anterior parts. From the capsule extend inward fine processes which form a delicate fibrous reticulum; within the reticulum lie the cells. These are situated for the most part very close together and constitute a real cellular cord. Sometimes they are arranged almost like glandular tubules. The cells are apparently of two kinds: the chief cells which we can stain with basic dyes (only slightly with acid) and chromophile cells, which are larger and which have affinity for such acid dyes as eosin. The eosinophile cells in the hypophysis cerebri of the cock are generally very scarce. The blood vessels consist almost entirely of capillaries which lie in a mesh work.

The weight of the pituitary bodies of 7 normal cocks is recorded in Table 1.

TABLE 1.

	Age.	Body Weight.	Hypophysis weight, gms.	Weight of 2 testes, gms.
1	6 months	0.720 Kg.	0.11	2.16
2	6 months	0.600 Kg.	0.16	4.00
3	1 year	1.300 Kg.	0.13	9.00
4	3 years	3.200 Kg.	0.14	20.00
5	3 years	2.000 Kg.	0.12	16.00
6	3 years	2.600 Kg.	0.14	18.00
7	3 years	2.500 Kg.	0.18	16.00

The pituitary bodies of 4 capons were found to average heavier in weight than those of the roosters. The hypophysis of the capon is far richer in the eosinophile cells than that of the rooster; it is also more hyperemic. The data pertaining to this series are comprised in Table 2.

TABLE 2.

Weight of pituitaries of 4 capons:

	Approximate Age at Castration, mos.	Weight at Castration, Kg.	Weight of testes, gms.	Interval, months.	Weight at Autopsy, Kg.	Weight of Pituitary gms.
1	6	0.720	2.16	6	1.500	0.260
2	6	0.748	2.00	6	1.800	0.225
3	6	0.500	0.50	6	1.800	0.275
4	6	0.750	2.20	6	1.600	0.262

Castration then produces, as was observed by Fichera, a hypertrophy of the pituitary body and an increase of its eosinophile cells. But I believe, if the increase of the eosinophils in the gland signifies its greater activity, we could have eosinophilia also in other conditions. Indeed, I have found a certain degree of eosinophilia in the hypophysis cerebri of the 6th and the 7th roosters (the roosters were perfectly healthy) and Vassale found that the pituitary body of the puppy has more eosinophils than that of the adult. Therefore, perhaps, the eosinophilia may be related to the skeletal growth.

C. RESULTS OF LIGATION AND RESECTION OF DUCTUS DEFERENS IN ROOSTER

(I.) From a young rooster about 75 days old and weighing 0.550 Kg. was removed (June 4, 1910) the right testis (weight 1 gm.); the left spermatic duct was ligated and resected. The animal developed like a normal rooster. January 18, 1911, the animal (weight 0.950 Kg.) was killed. At the autopsy the left testis (weight 0.75 gm.) was found smaller and harder than the normal. In the epithelinin of the tubules degenerative changes were noted; the tubules were smaller than normal. In a few seminiferous tubules some spermatozoa still remained. The interstitial connective tissue was slightly increased and in this tissue the Leydig's cells were increased in number.

The pituitary body weighed 0.215 gm.; it was heavier than normal, but did not reach that of the capon. The quantity of the eosinophile cells in the pituitary was normal.

(II.) In a young rooster (weight 0.900 Kg.) about 6 months old (November 16, 1912), ligation and resection of

both spermatic ducts was carried out. The animal developed normally. June 18, 1913, the rooster was killed (weight 1.450 Kg.). At autopsy the right testis weight 3 gm., viz., less than the normal; the left testis was very small and weighed 0.20 gm. The pituitary body weighed 0.2 gm. The study of this experiment was interrupted; the microscopical examination of the testis and pituitary body was not made. It is included as showing atrophy of the testis.

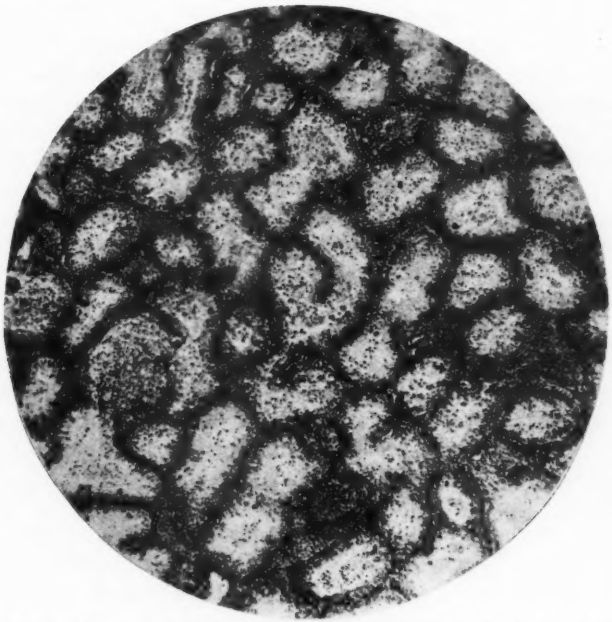

Fig. 2—Testis of cock, Series C, Experiment I, after ligation and resection of spermatic duct. Shows some spermatozoa in a few seminiferous tubules and degenerative changes in its epithelium, slight increase of the interstitial connective tissue and the Leydig's cells. Fixation, Bouin's fluid; staining, haematoxylin-eosin; magnification, 60 diameters.

(III.) In a young rooster (weight 0.850 Kg.), age 6 months (November 18, 1912), ligation of both spermatic ducts was carried out; they were not cut. The bird grew normally. June 18, 1913, the rooster, in good condition, was killed (weight 1.700 Kg.). At autopsy it was found that the ligature had yielded; the ducts were open. Together the testes weighed 5.25

gm. They appeared normal. The pituitary body weighed 0.215 gm. It was normal in structure.

(IV.) In a rooster one year of age (weight 2.050 Kg.) ligation and resection of both spermatic ducts was carried out (January 6, 1920). The animal recovered in a few days. February 29, 1920, the rooster (weight 2,400 Kg.) was in good health. A laparotomy was done and it was found that the left ductus deferens was reconstructed and its testis normal. The left testis was removed (weight 11.00 gm.). The right testis appeared small and seemed harder than normal; its vas deferens was also small. The animal recovered slowly. March 20th, the animal was well, but it seemed that its secondary sexual characteristics were less marked than normal. The crowing was not clear and strong. April 16th, the animal was in good health; a third laparotomy was made. It was very difficult to ablate the testis because the gland was sclerotic. It was removed in pieces. After the operation the rooster recovered in a few days, but at the same time it ceased to crow, lost its sexual instincts and the desire to fight.

The animal, when killed, weighed 2.530 Kg. The left testis (the first removed) was normal. The right testis (the second removed) showed: (a) the spermatogenetic cells with degenerative changes; (b) the Sertoli's cells normal; (c) a few spermatozoa; (d) increase of connective tissue and a slight decrease of Leydig's cells; (e) edema, hyperemia, lymphangitis and infiltration as in chronic orchitis. The loss of the left testis and the decrease of the Leydig's cells in right testis after the first operation may be the explanation of the diminished male instincts. The pituitary body weighed 0.23 gm. Microscopic examination showed a marked increase of the eosinophile cells.

(V.) Rooster, age about 3 years (weight 3.200 Kg.); January 9, 1920, both spermatic ducts were ligated and resected. The animal recovered in a few days; it remained male in its attributes. March 4th, the animal was in good condition. A laparotomy was done; the spermatic duct appeared small and almost empty. The testes were small, but the right testis was larger than the left. The right testis was removed. In one week the animal recovered and showed no changes in the secondary sexual characteristics.

April 8th, the animal (weight 3.100 Kg.), showing all the male characteristics, was killed. At autopsy the left testis (weight 2 gm.) was small and hard. The pituitary body weighed 0.18 gm. Microscopic examination of the right testis (which was removed March 4th) showed the seminiferous tubules smaller than normal; in the lumen were found a very few spermatozoa. It seemed that spermatogenesis had stopped. The spermatogenetic cells did not show important degenerative changes. There was marked hyperemia. The interstitial connective tissue was increased as well as the interstitial cells. The right spermatic duct contained no spermatozoa. The seminiferous tubules of the left testis were smaller than those of the right; nevertheless it was possible with careful search to find a few spermatozoa. Almost all of the spermatogenetic cells showed marked atrophy. The interstitial cells were slightly increased in number. The left ductus deferens was small; its epithelium was atrophic and no spermatozoa were found in the lumen. Very few eosinophile cells were found in the pituitary body.

(VI.) In a rooster age two years (weight 2.900 Kg.), on January 24, 1920, both spermatic ducts were ligated and resected. In a few days the animal recovered. March 30th, the rooster was quite well (weight 2,950 Kg.). The abdomen was opened and the right spermatic duct was found to be closed; it appeared greatly swollen; the left spermatic duct was reconstructed. We hoped to repeat the operation, but the rooster died.

At the autopsy the left testis (weight 11 gm.) appeared normal; the right, which had the duct closed, appeared the larger (weight 22 gm.). On microscopic examination of the right testis the seminiferous tubules appeared swollen with spermatozoa; the tunica albuginea was extremely extended. The spaces between the seminiferous tubules were large; there was edema in the testis. The pituitary body weighed 0.18 gm. The eosinophile cells were normal in quantity.

(VII.) In a rooster, age two years (weight 1.775 Kg.), on January 26, 1920, ligation and resection of both ducts was carried out. The animal recovered in a few days. April 22nd, the animal was in good health and had kept its secondary sexual characteristics and male instincts. A laparatomy was done; the

ducts were still obstructed and full of the testicular secretion. The left testis was removed (weight 11 gm.). The testis that remained appeared larger than normal. During the days following the operation the animal became very ill. It recovered slowly; but seemed to preserve its male instincts. It fought with other roosters, although very weak (May 5, 1920). On June 1st, the rooster had recovered, but it was yet weak. On June 3rd, it was killed.

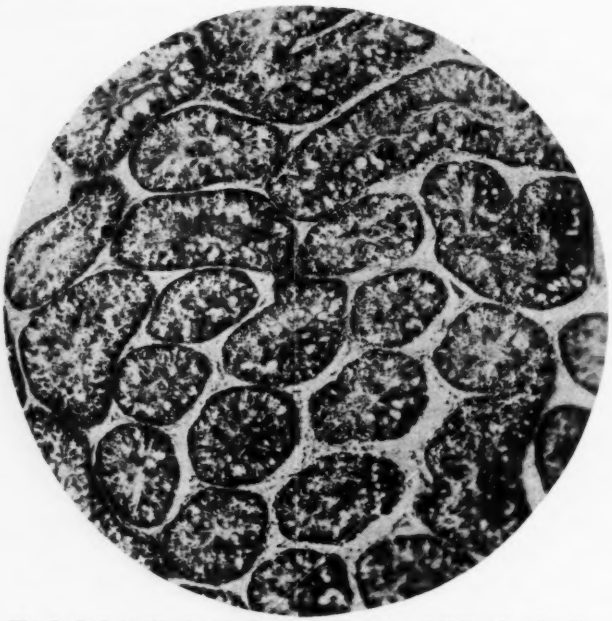

Fig. 3—Left testis of cock, Series C, Experiment VII., after ligation and resection of spermatic duct. Seminiferous tubules dilatated and full of spermatozoa; hydropic degeneration of the epithelium of the seminiferous tubules; interstitial connective tissue increased; Leydig's cells in normal number; edema. Fixation, formalin; staining, haematoxylin-eosin; magnification, 60 diameters.

At autopsy the right testis was found very small and harder than the normal (weight 2.50 gm.). The pituitary body weighed 0.17 gm. Microscopic examination showed that the left testis, which had been removed April 22nd, had the seminiferous tubules dilated and full of spermatozoa of which many displayed degenerative changes. There was hydropic degeneration of its

epithelium; the interstitial connective tissue was increased; the Leydig's cells were normal in number; the organ was edematous. The right testis showed no spermatozoa in the seminiferous tubules, which were retained; the epithelium showed marked degenerative changes; there was a marked increase of the interstitial connective tissue and increase of the number of the Ley-

Fig. 4. Right testis of same cock as shown in Fig. 3. Note absence of spermatozoa in the seminiferous tubules and marked degenerative changes in their epithelium; marked increase of the interstitial connective tissue and increase of the number of the Leydig's cells. Fixation, formalin; staining, haematoxylin-eosin; magnification, 60 diameters.

dig's cells. The epithelium of the vas deferens showed extensive degenerative changes and marked increase of the fibrous coat. The pituitary body showed an increase in the number of the eosinophile cells; this, of course, may have been due to the infection to which the rooster had been subject for a long period of time.

(VIII.) In a rooster, age about two years (weight 2.900 Kg.), January 27, 1920, ligation and resection of both spermatic ducts was performed. The animal recovered in a few days, but was always weak; it kept its secondary sexual characteristics. On February 22, 1920, it was killed (weight 1.650 Kg.).

Fig. 5. Testis of cock, Series C, Experiment IX, after ligation and resection of spermatic duct. Shows edema throughout the testis; hydropic degeneration in the epithelium of the seminiferous tubules, which are distended and full of very numerous spermatozoa; Leydig's cells normal. Fixation, formalin; staining, haematoxylin-eosin; magnification, 60 diameters.

At autopsy no infection in the abdominal cavity was found. The cause of the weakness remained unknown. The testes were small; the right weighed 1.10 gm.; the left, 1 gm. The vasa deferentia were obstructed. The pituitary body weighed 0.15 gm. Microscopic examination of the testis disclosed albuminous degeneration and atrophy of the epithelium of the seminiferous tubules; no spermatozoa were present. A marked increase of the interstitial cells was found. The pituitary body was normal.

The atrophy of the testis was due probably more to the general condition of the animal than to the effects of the operation. But what is important from my standpoint is that the animal always preserved the male characteristics. For this reason the experiment is included in this series.

(IX.) In a rooster, age about three years (weight 2.700 Kg.), January 30, 1920, ligation and resection of the ductus deferens was performed. The animal recovered in a few days following the operation. The ducti deferentii were obstructed. During an attempt to remove a testis the animal died.

At autopsy it was found that each testis weighed 22 gm., and the pituitary body, 0.15 gm. On microscopic examination of the testis the following were noted: (a) edema in all testis; (b) hydropic degeneration (vacuolisation) in the epithelium of the seminiferous tubules; (c) very numerous spermatozoa in the seminiferous tubules, which were distended; (d) the Leydig's cells were normal. The pituitary body also appeared normal.

(X.) In a rooster about two years old (weight 2.900 Kg.), February 3, 1920, ligation and resection of the spermatic ducts was carried out. During the operation the right ductus deferens was accidentally ruptured near the kidney. It was not possible without risk of killing the animal to reach the duct again; it remained pervious so that the semen was poured into the peritoneum. In a few days following the operation the animal recovered. March 28th, the rooster was in good health. The right testis was ablated. The left testis felt larger than normal. The animal in the following days recovered and preserved completely its secondary sexual characteristics and instincts. The right testis was normal. On May 18th, during an operation for removal of the left testis, the rooster died. The testis was harder than normal; it weighed 12 gm. The pituitary body weighed 0.1 gm.

On microscopic examination the following observations were made: (1) the right testis was normal (the first removed and which had the vas deferens accidentally broken. (2) The left testis showed: (a) the seminiferous tubules swollen by spermatozoa; (b) hydropic degeneration of the epithelium lining the seminiferous tubules; (c) the lumen of the seminiferous tubules not distended; (d) the interstitial connective tissue in-

creased and the Leydig's cells more numerous than normal. (3) The pituitary body showed few eosiniphile cells.

The increase of the interstitial connective tissue explains why the left testis was harder than normal; probably this state represents the beginning of the sexual period, when the testis becomes atrophic because of the sclerosis of the interstitial connective tissue. (See Exp. I.)

(XI.) In a rooster about two years old (weight 2.320 Kg.), on February 11, 1920, ligation and resection of the spermatic ducts was done. The animal recovered in the days following. April 27th, the animal (weight 2.400 Kg.) was well. The peritoneal cavity was opened. The spermatic ducts were found to be reconstructed; the testes appeared normal. The left testis was removed; the right was distributed in peritoneum, divided in small parts. The animal died after two days, due to infection of the peritoneum.

On microscopic examination it was found that the pituitary body had numerous eosinophile cells. This eosinophilia might have been due to diminished testicular internal secretion (of the testes, one was removed and the other was spread in the peritoneum) or by the infection.

The foregoing data show that after ligation and resection of the ductus deferens we can have the following results:

1. The ductus deferens may be reconstructed (See Exp. IV, VI, XI; in Exp. III only ligation was done). In these cases we have no changes in the testis.

The ductus deferens may remain obstructed, but the consequences in the testis are not always the same: (a) sometimes following the operation the vas deferens and the testis increase in volume. After three months the testis may become enormous (See Exp. VI, VII, IX). On microscopic examination of the gland we find the seminiferous tubules greatly dilated and containing an extraordinary number of spermatozoa. Numerous spermatozoa are found in the vas deferens. In the epithelium of the seminiferous tubules we find hydropic degeneration. The interstitial connective tissue and Leydig's cells are normal or slightly increased; the testes are edematous throughout. To this first period succeeds a second (See Exp. I, II, VII, X) marked by increase of the interstitial connective tissue followed by

atrophy of the testis. After 4 or 5 months the seminal gland has become harder than normal and very small. On microscopic examination the seminiferous tubules appear small and the spermatogenetic function greatly diminished or almost disappeared.

At times, on the contrary, we have early atrophy of the testis. The gland becomes smaller and harder (Exp. IV, V, VIII); on miscroscopic examination we find the seminiferous tubules smaller and degenerative changes in spermatogenetic cells; few of these complete their cycle so as to become spermatozoa. The Leydig's cells, on the contrary, remain normal or increase in number. The time necessary to have these results varies within two or three months. I believe that the early atrophy seen in these cases depends upon the fact that during the operation the nerves which follow the vas deferens are injured. Marrassini, who obtained the same results in dogs by the ligation and resection of the ductus deferens, offers such a hypothesis. This author did not consider the consequences of the operation on the secondary sexual characteristics. Researches to establish the etiology of the different results will be undertaken in dogs in which it is easier to operate and to follow the consequences of the operation. But the important observations as regards the scope of the present study are that in no case in roosters after ligation and resection of the ductus deferens did there occur changes in the secondary sexual characteristics; in case of young animals development was normal (Exp. I, II). The observations of Ancel and Bouin in the rabbit are thus confirmed in the rooster. But the removal of the atrophic testes in which the Leydig's cells were in good condition (as confirmed by microscopic examination) caused in the adult animal a sudden cessation of crowing, a loss of the sexual instincts and of the desire to fight; I have observed no other changes.

The study on the hypophysis cerebri has shown that until the atrophic testis is removed, the organ in the rooster does not undergo the changes characteristic of castration (See Exp. I, II, V, VIII), but after its removal the pituitary body presents the same changes we have observed in the capon (See Exp. IV). Apparently then the hypophyseal changes are due to loss of the internal secretion of the testis. In the pituitary body of the

roosters of Exp. VII and Exp. XI the number of the eosinophile cells exceeded the normal, but was less than in the capon. In the pituitary body of normal roosters we can find sometimes, as we have seen, a certain degree of eosinophilia. Such eosinophilia can also be the consequence of infection from which the animals have suffered.

D. CONSEQUENCES OF THE TRANSPLANTATION OF TESTICULAR TISSUE IN THE ROOSTER

This research was undertaken to determine the eventual changes occurring in testicular tissue (particularly the Leydig's cells) transplanted in the peritoneal cavity and the relation of such transplantation to the secondary sexual characteristics and sex instincts. The operation was the removal of both the testes and the division of one into small pieces, which were scattered upon the peritoneum.

(I.) A young rooster about five months old, weighing 750 gms., was operated upon June 5, 1909. Complete removal of both the testes from their normal position was accomplished. The left testis weighed 1.5 gm. The right testis, which was about the same weight, was scattered about the peritoneum. The animal in the days following recovered, but crowed like a capon. On January 10, 1910, the animal, presenting the appearance of a capon, was killed. At the autopsy no trace of the testis was found in the abdominal cavity. The pituitary body weighed 0.230 gm. On microscopic examination the organ was found to present the picture typical of the capon.

(II.) A rooster weighing 2.017 Kg., about one year of age, was operated upon January 5, 1920. The removal of both testes was attempted. A small part of the left testis (weight 3 gm.) remained in situ (approximately 1/20 of the gland). The right testis was scattered about the peritoneum. In a few days following the operation the animal recovered. On March 1st, the animal, which now weighed 2.50 Kg., was killed.

Autopsy disclosed that the residue of left testis was in normal condition and two nodules of the testis which had been scattered about (right testis) had become adherent to the peritoneum. The pituitary body weighed 0.22 gm. On the microscopic examination the vestiges of the testis showed numerous spermatozoa in the seminiferous tubules and hydropic degenera-

tion of its lining epithelium; the interstitial connective tissue and its Leydig's cells were normal; some edema was evident.

The pituitary body showed an increase of the eosinophile cells. During the operation the rooster had lost almost all the left testis, and of the right, which had been transplanted, only a part remained grafted on the peritoneum. The microscopic examination showed no increase of the interstitial cells in the residue of the left testis nor in the transplanted testicular tissue. The small number of the Leydig's cells in the body of the animal can explain the diminished crowing and male instinct and the moderate hypertrophy and eosinophilia of the pituitary body.

(III) A rooster weighing 2.460 Kg., about two years old, was operated upon May 6, 1920, both testes being removed. The right testis was morcellated and scattered in the peritoneum. The left testis weighed 16 gm. In the days following the operation the animal recovered but lost the sexual and the fighting instincts. He never was observed to crow. On June 8th, the animal, in good condition, was killed.

At the autopsy no traces of the testicular substance were found. A few nodules adherent to the peritoneum were taken for histological study, but they were found to be made up of fat only. The pituitary body weighed 0.27 gm.

* * * * *

These experiments indicate that it is occasionally, but by no means always, possible to graft testicular substance upon the peritoneum. Where a successful graft is made the tissue after some time undergoes degenerative changes that involve all the elements of the structure. With the progress of the degenerative changes the sexual instincts diminish. Since the degenerative changes involve all the testicular substance it is not possible to distinguish clearly which of the two, Leydig's cells or epithelium of the seminiferous tubules, gives rise to the internal secretion. For this reason researches along this line were not continued.

Concerning the scientific question of the utility of the transplantation of the testis in old men, which, according to Stanley and Keller, produces in the body beneficial effects, I am of the opinion that exciting the sexual activities can produce only unhappy effects. The extinction of the sexual function in

old age is a physiological phenomenon accompanying the decay of the several functions of the body. The body organism is tired and if life is to continue there is need of rest and the conservation of the failing strength, which is not to be spent as in youth. Now it is notorious that sexual activity consumes much energy of the body, and wastes various substances, especially the lecithin, necessary to the nerve tissue. The consequences to the brain of sexual excess (v. Frankl-Hochwart) are well known and to create anew the sexual function by transplantation of the testes into the body, which has abolished this function because it has become old, is to contravene the normal laws of nature.

DISCUSSION AND CONCLUSIONS

The results of the work herein reported may be summarized as follows:

I. The testis has an internal secretion, which gives to the male the masculine sexual characters and sexual instinct and keeps the function of the hypophysis normal. This is well shown by the changes that come in the secondary sexual characteristics and in the pituitary body after castration and by the fact these changes do not come when there remains in situ or in the peritoneal cavity some part of the testis in functional condition. The nervous theory (Pflüger, Samuel) fails then, although some facts according to Luciani can find explanation on this theory which cannot find an explanation on a theory of internal secretion.

II. In the testis we have the spermatogenetic cells in the seminiferous tubules and the Leydig's cells in the interstitial connective tissue. Which of the two, then, produces the internal secretion? My researches indicate that the Leydig's cells have the endocrine function. This conception is supported by the following facts: (1) The Leydig's cells have the characters of secretory cells in that they elaborate fatty granules and mitochondria. (2) The animal remains normal even when we have marked atrophy of the seminal epithelium (See Series C, Exp. I, V, VII, VIII). (3) It is only when we remove the atrophic testis with the Leydig's cells then in good condition, that we have the changes that are noted after castration (See Series C, Exp. IV). (4) No facts exist which speak for the conception that the spermatogenetic cells exercise the endocrine function:

they complete a cytological cycle to become spermatozoa, which have merely the biological function of reproductive cells.

But the new information on the internal secretion of the testis that shows the effects of its abolition is very important not only for itself, but also because it shows that there exists through the internal testicular secretion a functional correlation between the testis and hypophysis cerebri. It lends support to the view that the pituitary body has the function of ruling the skeletal growth, and perhaps throws some light upon the obscure etiology of gigantism and acromegaly. In the acromegalic there is found marked hypertrophy of the hypophysis with eosinophilia of its cells and deficient development of sexual organs (Benda, Vassale, Cushing). But in the acromegalic the more important fact is that it is a lesion (hypertrophy, adenoma) of the pituitary body, whereas in the castrated it is the loss of the internal secretion of the testis, which secondarily produces hypertrophy of the hypophysis.

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EFFECTS OF X-RAY TREATMENT OF THE HYPOPHYSIS IN BRONCHIAL ASTHMA

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In the insufficiency of the endocrine organs the only therapeutic means, in use heretofore, with the exception of the casual treatment in specific cases, have been opotherapeutic substitutions. The results of such measures are at times wonderful, though often they prove disappointing, while the cause of failure can not always be determined. Long ago we thought of another way to correct endocrine insufficiencies through stimulation of the specific glandular elements; as a means to this end we chose deep radiations with x-rays.

Hitherto radio-therapy in endocrinology has been used only in destroying tissue, as in cases of exophthalmic goitre, in tumors of the hypophysis, etc. It remained to be seen whether, with lighter applications, the opposite effect could be reached of stimulating the gland cells to activity, or in other words if a *stimulating endocrine radio-therapy* were possible.

As soon as the necessary apparatus was available we tried the practical application of the principle suggested. The first treatment, made last January, was made in a case of dystrophy adiposo-genitalis.

The patient (B. P. a boy of 15) showed marked adiposity of the thighs, buttocks, mons veneris, breasts and inferior quadrant of the abdomen. His genitalia and secondary sexual characters were but slightly developed. The penis was 5 cm. in length and almost buried under the suprapubic fat; erections were infrequent and incomplete. There was no sexual tendency and no hair at the axillae, pubis and perineum. The voice was infantile. The body was underdeveloped; he was 1.49 m. in height and had short heavy limbs. Radiographically, no appreciable enlargement of the sella turcica could be detected. The patient had undergone several months of pituitrine and endospermine treatment with hardly any improvement; in one year

the penis had grown but 1 cm. in length and the height had increased only 2 cm. No hair had developed.

At the beginning of this year the patient had four irradiations of the hypophysis at intervals of one month. At every sitting three different fields were irradiated, one frontal and two temporal, for 36 minutes in all, at a distance of 45 cm., using an aluminum filter of 2 mm., S.E. 18-20 cm. and M.A., 3½. Twenty-five days after the first irradiation the pubis began to show hairs which gradually increased in number and length; the penis and testes increased in size, the penis in three months reaching a length of 8.5 cm. Erections became frequent and complete; the sexual tendency was accentuated. The height increased 5 cm. to 1.56 m., and the fat tended to diminish; the chest measurement dropped from 86 to 81 cm.

The irradiation treatment was also tried in a case of scleroderma. The patient, C. P., was a woman of 58. Her lesions, dating back two years, were especially conspicuous at the lower part of the thorax and superior part of the abdomen; the affected area extended like wide ribbons around the trunk, 10 cm. in breadth, with extensions upward to the breasts and downward to the pubis. Furthermore, there were oval and circular plaques, 3-5 cm. in diameter, on the breast, in the sternal region, the suprahyoid region, forehead and neck. The patient complained of diffuse pains in her body and limbs, great prostration, flushes of the face, slight tachycardia, anorexia, nausea, heavy feeling in the epigastrium and psychic sluggishness. Thyroid and hypophyseal treatment for six months had not modified either the general condition or the local lesions.

Then the patient underwent irradiations of the hypophysis as well as of the thyroid. Four treatments were given at intervals of about a month. Irradiation of the hypophysis was continued for 12 minutes in three different fields with the tube at 45 cm. distance, with a 2 mm. aluminum filter, S.E. 18-20, and with a current of 3½ ma. The thyroid irradiations lasted 5 minutes, with 2 mm. aluminum filter, S.E. 18-20, and current, 3 M.A.

After the second irradiation the cutaneous lesions began to change. The sclerodermic plaques of the breasts and suprahyoid region disappeared and the wide zone of affected skin, before shiny, copper-colored, thick and sticking closely to the under-

lying tissue, became pale, pink and thinner. It was possible to lift it in folds and the line of demarcation between the healthy and affected tissue became less apparent. The patient still complains of prostration and dyspesia, but the pains are greatly diminished, the pulse is slower and there is no more flushing of the face nor feeling of tension and weight in the abdomen. The psychic improvement is most marked.

Good results were also obtained in a case of Basedow's disease with two irradiations of the thymus. There was lessening of the tremor and the tachycardia (from 116-120 to 96-100) diminishing of the goiter (from 34 cm. to 31.1 cm) and subjective relief (15 minutes irradiation through 2 mm. aluminum filter, S.E. 20-22; M.A., 3).

Although in the above noted cases the effect has been satisfying, in other cases no defined result was obtained in regard to the fundamental lesion. A typical case of eunuchoidism in a patient of 26 was subjected to four applications to the testes and hypophysis and two to the thymus; a case of angioneurotic oedema of Quinke had three irradiations of the hypophysis and ovaries (in this case the general conditions improved and the menstruations became regular) and three cases of diabetes mellitus who had each four irradiations of the hypophysis and pancreas. In all these cases results were negative.

These negative results do not vitiate the principle predicated upon the positive results, and they should not hinder us from keeping on with the method. Other cases may improve under such treatment and, furthermore, given the delicate interweaving of mutuality, interference, antagonism and synergy existing between these glands, some modifications may be required, especially in regard to the Basedow cases and diabetes mellitus, which are now considered as pluriglandular syndromes.

It is also necessary to determine to what extent the irradiation may be used on the several glands to produce only the stimulating effect, a subject to be studied methodically and with prudence. Of course, there can not be obtained any stimulation whenever the tissue has degenerated to such an extent as to be no longer excitable.

We are sorry to have missed the opportunity of experimenting with irradiation of the hypophysis in diabetes insipidus, or of

the parathyroids in tetany maladies that seems especially to lend themselves to such treatment.

In view of the favorable results obtained by various observers in the use of pituitrin in asthma, irradiations of the hypophysis were tried in this disease. At each sitting three different fields were irradiated—one frontal and two temporal—for 12 minutes with aluminum filter of 2 mm., S.E. 18-20 cm. and 3½ M.A. current.

Case I. Frank G., 29 years old, a landowner, had been suffering from asthma for the past ten years. In the beginning the attacks lasted but a few minutes, coming on only once every 5-6 months. Since April of last year they had become very frequent—3 to 4 a day—so that the patient was hardly ever free from them and required 2-3 hypodermic injections every day of "asmolisina," which gave him some respite. Furthermore, every 7-8 days there were severe periods which lasted 8-10-12 hours when the patient was forced to keep absolutely immovable, since any slight motion increased the spasm and he had to take 10 to 15 or even 20 injections a day of "asmolisina." He is the brother of a physician and by him was brought to us to see if anything could be done for relief.

The patient is not tall, but appears very strong, and there is nothing abnormal about him but a decided emphysema, getting worse with the asthma. On May 15th the radio-therapeutic treatment was begun. He was given in all five treatments at 7-day intervals. Two days after the first irradiation one of his usual periods began, but it was milder and shorter, 3 to 4 injections of "asmolisina" a day being enough to allow him to go about. After this crisis there followed 8 days of complete relief from symptoms. A few days after the third irradiation a new crisis, but even milder than the previous one occurred. The attacks came on every other day, one to two a day; no "asmolisina" was required. This period lasted about a week, after which for 8 or 10 days he was well. Recently a few attacks have been experienced, but only at night and of very slight severity.

Thanks to the treatment the patient now secures sure relief from the "asmolisina," which before was only partially and slowly efficacious.

Case II. N. S. is a woman 37 years old. Her history is unimportant. Asthma has persisted two years. It began with brief attacks, 20 to 30 days apart. Since last November there have been 4 or 5 a week, lasting 3 to 4 hours. "Asmolisina" proved more dangerous than useful. The first irradiation of the hypophysis was given April 2nd and followed by four others eight days apart. From the first application the asthma ceased except for a very slight attack of a few minutes each.

Case III. U. R. is a boy 15 years old, a student. He is poorly developed, but nothing important was learned in his history. The first attacks of asthma began when he was 3 years old; they were short and infrequent. For the past 16 months they have occurred every 15 to 20 days and lasted 4 or 5 days.

Four weekly irradiations were given. Two days after the first a slight attack lasing two hours was experienced. On May 30th another attack occurred, but lasted only a few minutes. Since that time he has been well.

Case IV. L. M., a housewife, is 42 years old. No abnormality was found; her general condition was good. The last 15 months she suffered attacks of asthma, at first every 10 or 15 days, lasting an hour, then the last 6 months, every day and lasting 3 to 4 hours. Pituitrin hypodermatically did not help her.

Three irradiations were given, May 6th, 21st and 28th. During the treatment three slight attacks of a few minutes each were experienced. From May 27th on she has been well, except for an infrequent slight cough with mucous expectoration.

Case V. G. G. is a man of 34, an electrician. His family history is unimportant. He had lues when 15 years old. In November, 1917, he had pleurisy of the left side. He was poorly nourished, the pleurisy not being well cured. He had also pulmonary emphysema and diffuse bronchial catarrh. During the past year he has had attacks of asthma every morning. Each attack lasted about half an hour. Irradiations were given May 20 and 27. The attacks were reduced to only two or three a week and these were short and slight. The bronchial catarrh was not modified.

In these five cases the influence of the irradiations is clear. In the opotherapeutic treatment of asthma usually pituitrin and adrenalin are used together, therefore, whenever the stimu-

lation of the hypophysis proves insufficient one should try the stimulating irradiation of the adrenals also.

At any rate, the above noted cases clearly demonstrate the usefulness of the treatment; as regards the duration of the application and the persistence of the effects we need further experience. At the same time we need to make sure that the effect is really due to stimulation of the hypophysis or if there be other factors acting on the syndrome. We shall try to determine any such by looking for the effects of these slight irradiations on the endocrine glands, studying the functional changes as we can in the present state of science.

It will be worth while trying through the irradiations to study the glands in their functional aspects already known as well as any new phenomena, which may be evoked.

The field is large and full of promise. Even in the treatment of certain tumors, the development of which is influenced by endocrine glands the irradiation of these glands may conceivably prove useful.

The foregoing researches are reported in their incomplete form because we are forced to interrupt them for reasons not under our control and because of other studies that are being made in the same field.

Stettner in two cases of arrest of development in centres of ossification through the x-rays applied to the head and to head and neck had good results, which he attributes to an endocrine factor (hypophysis.) In asthma, Klewitz irradiated the anterior and posterior thorax in 18 to 20 fields, though without any beneficial effect. Stephan, on the basis of researches on the irradiations of the spleen thinks that such methods may be applicable wherever there is any obstacle to the cellular functioning and consequently in endocrine dysfunctions. Fränkel in a recent meeting of the German Radiological Society, talking of the stimulating action of very slight irradiations expressed a belief that such treatment might prove successful in endocrine dysfunctioning.

Precisely this hypothesis has been the starting point of our researches and the data herein repeated indicate the validity of the hypothesis.

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A FATAL CASE OF CARDIAC DILATATION WITH ASSOCIATED GASTROPATHY AND ENDOCRINOPATHY

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The subject of this report was a robust, vigorous young woman, a brunette, who married at the age of 19. She was the child of healthy parents and had enjoyed perfect health herself. About sixteen months after marriage she gave birth to a normal appearing nine-pound boy. At two months of age the child developed infantile eczema of an extreme type, which, after some weeks of varied treatment, responded quickly to thyroid extract. The eczema returned each time the treatment was discontinued.

At seven months it was decided to wean the child and thereupon developed violent and unconquerable fits of anger upon his part. They came on suddenly and were so noticeable that my attention was repeatedly called to the condition. Soon thereafter a gradual enlargement of the head, increased adiposity, changes in the appearance of the skin and lips made the diagnosis of cretinism positive. The thyroid treatment was again instituted, with a gradual recovery over a period of some months.

Soon after lactation had ceased, the mother went away for a visit but was brought back in five weeks in a most serious condition. This she reported had begun to develop before leaving. She had lost much weight, was weak and very nervous. Her pulse averaged between 120 and 160. She was dyspneic on the slightest exertion,—in fact, at this time was unable to leave her bed. Her urine contained a large amount of sugar and her thyroid was palpable. After eight weeks the sugar had disappeared, her pulse had decreased to between 80 and 90. Three months later she had about recovered from the acute hyperthyroidism but was constantly watched. She became apparently well and happy.

A year later she became pregnant and through the entire gestation enjoyed perfect health, as in her former pregnancy. A girl was born but was taken from the breast soon after birth because of the previous experience with lactation. This child has never developed any symptoms or condition suggestive of glandular disease.

Without going into all details, suffice it to state that the mother developed nervous symptoms soon after the birth of this latter child. The chief of these were referable to her stomach and associated with sudden increases of pulse rate. The attacks came on usually at night, without regard to food. She complained of fulness, pressure around the heart, dread of fainting and rapid pounding of the heart. The attacks becoming more and more frequent and beginning to tell notably on her weight, she was ordered to bed for a rest cure and a complete examination was repeated. The thyroid was palpable but not to the same extent as during her former illness. The cardiac outlines were normal. The blood pressure ranged from 122 to 105 systolic and 85 to 65 diastolic. The urine was negative, as was the blood Wassermann. There was no exophthalmus or any other goiter signs. Operative procedures were opposed for the time by the family in an effort to try out the medical measures; this procedure was agreed to by me. Two infected teeth and the tonsils had previously been removed, with improvement of the patient's general condition for a time. Chronic appendicitis had been discovered some months previously.

Ten to twelve weeks later she was out again and relatively well except for the occasional attacks with her stomach, giving rise at times to only a transient feeling of suffocation. Her pulse remained within normal limits.

A few months later an acute attack of appendicitis developed one night. A surgeon was called and the entire history reported. After due deliberation, on account of the suddenness, the severity of the attack and a 22,000 lucocytic count, she was operated upon that night. A purulent appendix of bad type was removed and drainage was instituted. For the next five days her recovery was exceptionally good. Her pulse never passed 84. She laughed and joked and desired food. On the morning of the sixth day I was hurriedly called. She was

cyanotic, with pulse of 120, diffuse apical impulse and left cardiac border outside the nipple line, indicating a condition of acute cardiac dilatation. Stimulants and minute care resulted in no improvement. She gradually grew worse and died at nine that evening.

DISCUSSION

The points presenting themselves in this history are the defective thyroid condition in the child, giving rise to a hypofunction as indicated by the eczema and cretinism; the relief with the administration of the gland but more marked relief upon cessation of the mother's milk. Striking also was the development of a hyperthyroid function in the previously normal mother upon the augmentation of her ovarian function and discontinuance of lactation. Again during pregnancy, when ovarian activity was in a depressed phase, her condition became normal in every way, only to be disturbed after parturition, when ovarain function was again stimulated.

In this connection I want especially to mention the gravity in prognosis, which is not sufficiently emphasized, in cases of so called functional heart conditions or in heart conditions without physical findings, in which gastric symptoms predominate. The feeling of fulness, pressure around the heart and suffocative influences often described as neurasthenic, especially when associated with any increase of the pulse beat, should be looked upon with alarm. In my experience, whether the patients are young or old, the majority of them sooner or later die suddenly. And then the thought arises whether or not many of the diagnosed anginas and even acute dilatations do not originally arise from thyroid intoxications which may or may not have been previously discovered.

525, The Woodward.

THE INFLUENCE OF THE THYROIDS ON THE FUNCTIONS OF THE SUPRARENALS

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INTRODUCTION

An attempt to analyse the literature dealing with the influence of the thyroids upon the suprarenals reveals the presence of difficulties which are due to a variety of causes.

The dual nature of the thyroids and parathyroids was not always appreciated by the earlier investigators, and conditions following parathyroidectomy have been ascribed to loss of the thyroids alone. Less confusion has existed with regard to the suprarenals, where cortex and medulla are anatomically even more closely related than are the parathyroids with the thyroids. From the points of view of development, structure and functions, the cortex and medulla of the suprarenals are generally regarded as distinct organs, though the possibility of some physiological interdependence of both structures is not excluded.

Another difficulty lies in the fact that the medulla of the suprarenals is composed of cells which are not confined to this situation. The occurrence of aberrant glands as a fertile source of error in experimental work upon the thyroids and parathyroids has long been recognized, but too little attention has been given to the same difficulty in connection with chromaphil tissues.

Swale Vincent (69) has described the anatomical distribution of the chromaphil tissues in many species of animals, and it has been shown by Fulk and McLeod (21) that extracts of the retro-peritoneal tissues of man, the dog, cat, rabbit, white rat,

calf, sheep and pig have the same physiological action upon intestinal and uterine muscle as the active principle of the medulla of the suprarenal gland. The exact proportion which exists between the adrenalin content of the suprarenals and that of the other chromaphil tissues has not been ascertained, and is probably variable even in the same species of animal, but it is a factor which cannot be entirely disregarded.

Considerable doubt still exists as to the exact nature and extent of the rôle played by adrenalin in the physiological processes of the body. Following upon the earlier work of Cannon and de la Paz (8), Cannon and Hoskins (6), and Elliott (18), a tendency to exaggerate the influence of adrenalin has been followed by the opposite extreme. Stewart and Rogoff (64) in the course of a long series of carefully conducted researches find little evidence that secretion of adrenalin plays any important part in the ordinary mechanism of the body, and these authors believe that adrenalin is not indispensable. Gley and Quinquaud (26) have arrived at a similar conclusion. Cannon (5) gives excellent reasons for regarding the secretion of adrenalin as fulfilling an emergency function. The recent work of Kellaway (37) and Bazett (3) tends to support the earlier views that the secretion of adrenalin is not unimportant, and the "tonus" theory receives fresh support from Bazett's observations. The question cannot be considered as finally settled.

A due appreciation of the influence one gland has upon the functions of another is necessarily limited while we are still in ignorance of the exact functions of each of the endocrine glands. In experimental work and in disease, it is difficult to determine how far the changes met with are due to alteration in activity of any one gland. The picture which results is often a syndrome in which there is a disturbance of balance affecting many organs. An observed change in one gland may appear to be due to excess or diminution of function of another when the real determining factor lies in the disturbance of a third gland or series of glands, or in some general change of metabolism.

The literature relative to the action of the thyroids upon the functions of the suprarenals is not free from contradictory statements. Some of the discrepancies are explainable, others need the test of experience to prove which is true.

The present paper makes no pretence to be an exhaustive survey. The literature is widely dispersed, much of it is difficult of access, and valuable contributions may have been overlooked. It is hoped that a summary, however imperfect, will have some value in showing the general trend of opinion on the subject, and that it will draw attention to the more salient features which require further experimental investigation.

II. The Effect of Hyperthyroidism on the Size, Weight and Structure of the Suprarenals.

R. G. Hoskins (33) in 1910 fed 28 female guinea pigs with commercial desiccated thyroid in small doses for varying lengths of time. Pregnancy occurred in many of the animals, but in most cases the offspring were premature or born dead. In 21 offspring which survived, the suprarenals were smaller than in the young of normal animals of similar age, the average loss of weight being 53 per cent. No histological differences in pigment, mitoses, or proportion between cortex and medulla were noticed. Hoskins interpreted the results as indicating a reaction in the suprarenals of the offspring to an increase of adrenalin in the maternal blood brought about by experimental hyperthyroidism.

In a further series of experiments Hoskins fed young guinea pigs from the day of birth on small quantities, 5 to 15 mg., of desiccated thyroid, beginning with the lower dose and gradually increasing. At the end of 15 days the animals were killed and the suprarenals compared with those of normal animals of the same sex and age. The suprarenals of the thyroid-fed guinea pigs averaged 25 per cent. heavier than those of the normal animals. Hoskins recognized a source of error in the possible presence of toxic material in the desiccated thyroid, but in other respects his experiments were carefully and suitably controlled. His conclusions were that hyperthyroidism stimulates the suprarenals to hyperplasia.

Iscovesco (35) prepared an ether-soluble material from the thyroid glands, which, when repeatedly injected into rabbits produced in addition to changes in other organs a notable hypertrophy of the suprarenals in both sexes.

E. R. Hoskins (32) in 1916 published the results of a very careful and complete analysis of the effects of thyroid feeding upon the growth of the body and organs of the albino rat. He

obtained as a result of thyroid feeding an overgrowth in the absolute weights of the suprarenals of 14.5 per cent. in the younger females, of 16.1 per cent. in the older females, of 36.4 per cent. in the younger males, and of 38.1 per cent. in the older males.

Herring (27) employing rather larger doses of thyroid than E. R. Hoskins, obtained even greater hypertrophy of the suprarenals. For the male rat the increase in weight of the suprarenals averaged 56 per cent, for the females 41 per cent, the largest individual increase being 140 per cent in the male, and 94 per cent in the female. Herring pointed out that the increase is mainly one of cortex, though there is also some hypertrophy of the medulla as shown by the greater depth and extent of staining of the chromaphil material. Herring also drew attention to the hypertrophy of accessory suprarenals which takes place under the influence of thyroid feeding. These bodies are not merely cortical, but in the albino rat frequently contain masses of chromaphil cells.

Kuriyama (41) in 1918 failed to obtain the results of the previous observers. Working also with the albino rat he stated that "thyroid feeding of either short duration with large doses, or long duration with small doses, does not materially change the epinephrin content, nor the weight of the adrenals of medium sized albino rats."

Hewitt (31) has recently confirmed the results obtained by Herring and Hoskins, and brings forward evidence to show that in the young albino rat after the cessation of thyroid feeding there is a tendency with the subsequent growth of the animal for the suprarenals to regain their normal proportions.

Kuriyama's experiments are unsatisfactory in that he employed desiccated thyroid of unknown activity in doses which would be toxic if fully active. His animals were of widely-differing ages and weights; the male and female rats were grouped together. Further, the diet given, dog biscuit and lard paste, is not above the suspicion of being deficient in vitamine.

Desiccation, if not properly carried out, may injure the active principle of the thyroid. Gley (23) found that the activity of organic extracts diminishes rapidly the higher the temperature used in their preparation. Swale Vincent (68) has noted the possibility of impairment of dried extracts by methods which

degrease
decrease them. Hewitt (31) has shown that commercial preparations of desiccated thyroid vary greatly in activity.

According to Carlson, Rooks and McKie (9), many of the symptoms induced by thyroid feeding are caused by an excessive protein diet and are not specific. This objection was avoided by Hoskins in that he used very small doses of thyroid and gave similar amounts of thymus and other organs to his control animals. Herring employed fresh ox thyroid in his experiments and gave similar amounts of fresh ox flesh to his controls. In none of the control animals were the specific reactions of the thyroid-fed groups observed.

R. G. Hoskins, E. R. Hoskins and Herring all found that the reaction of the suprarenals to thyroid feeding is greater in the male rat than it is in the female. In the normal animal it must be remembered that the suprarenals of the male rat are lighter per unit body length or body weight than those of the female. The curve of growth, too, of the suprarenals differs considerably in the two sexes (Donaldson, 16). For these reasons alone male and female animals should be separately grouped for experimental work.

McCarrison (45) has shown that the absence of certain vitamines from the food induces hypertrophy of the suprarenals with loss of adrenalin. It is therefore of importance that all animals used for experimental work should receive both before and during the investigation a liberal supply of fresh and suitable food. It is also advisable that the thyroid-fed animals and their controls should be paired from the same litters to avoid as far as possible individual variations.

Cramer (12) has advocated the view that the cortex of the suprarenals, and particularly its zona reticularis, takes part with the medulla in the formation of adrenalin, and that the cortex and medulla are not functionally independent of one another. By a method of staining with the vapour of osmic acid he has demonstrated granules in the zona reticularis which appear to be of the same nature as the adrenalin granules. Cramer also finds that conditions producing overactivity of the thyroids increase the size of the suprarenals and lead to changes in the distribution of fat in the cortex, and to a diminuation of the adrenalin granules in the medulla. Such changes are, however, acute and were brought about by poisoning with β-tetrahydronaphthyla-

ERRATA:

Page 581, line 1: Read "degreased" for "decreased."

mine, a drug which Elliott (18) proved to cause a rapid discharge of adrenalin from the suprarenals.

There are very few references in the literature to the action of thyroid upon the cortex of the suprarenals. F. Munk (50) noticed a diminution of lipoids in the cortex of the suprarenals of animals which had been thyroid-fed.

The balance of evidence is in favour of the view that the administration of small doses of thyroid brings about hypertrophy of the suprarenals. The cortex of the gland is the part primarily affected, and the histological changes require further investigation. There is also some evidence that the medulla of the suprarenals and the chromaphil tissues generally, participate in the enlargement.

It is doubtful how far the hypertrophy of the suprarenals may be attributed to a direct action of the thyroid hormone upon these organs. It is possible that, as postulated by Eppinger, Falta and Rudinger (19), thyroid has a stimulating action upon tissues which produce adrenalin, but the relatively greater hypertrophy of the suprarenal cortex is more likely to be induced by indirect factors. The gross enlargement of liver, pancreas, heart and kidneys which occurs in thyroid-fed rats points to a general disturbance of metabolism which may be responsible for the condition. Further work is necessary to elucidate these changes.

III. The Effect of Hypothyroidism upon the Size, Weight and Structure of the Suprarenals.

Marinesco and Parhon (48) in 1908 studied the changes which take place in the fatty material of the suprarenal cortex in dogs deprived of their thyroids. They described two varieties of fat, and found that there was a notable diminution in the amount and size of the lipochrome droplets, more especially in the cells of the zona fasciculata. They regarded the cortex of the suprarenals as being especially concerned in the elaboration of lecithin and allied bodies, and concluded that this function is modified by thyroidectomy.

R. G. Hoskins (33) thyroidectomised newly-born guinea pigs, but found no subsequent change in the weight of the suprarenals compared with those of normal animals of the same age.

Lorand (44) stated that in senile myxoedema atrophy of the thyroid is followed by regressive changes in other organs of the body of which the suprarenals are examples.

Gley (24) found that the suprarenals of thyroidectomised rabbits are notably hyperthrophied and full of fat, but he regarded this condition, not as a sign of hyperfunction, but of degeneration of the cells in the last stages of myxoedema.

Herring (28) noted that in male adult rabbits killed from 30 to 73 days after thyroidectomy the suprarenals were lighter per unit body weight than were those of control rabbits of the same sex. The suprarenals were used for the determination of their adrenalin content so that no histological examination was made. The animals appeared to be perfectly healthy when killed.

F. W. Mott (49) in the investigation of the pathology of myxoedema described a case in which the suprarenals showed a marked diminution of the lipoid contents of the cortex.

Cramer (14) stated that removal of the thyroid gland in rats and rabbits produces histological changes in the cortex which are, however, only slight, and appear to indicate a disturbance in the secretory mechanism of the gland rather than a deficiency in the formation of adrenalin.

The effects of hypothyroidism upon the suprarenals requires further investigation, and no definite conclusions can be drawn from the small number of observations quoted.

IV. The Effect of Hyperthyroidism upon the Adrenalin Content of the Suprarenals.

In estimations of adrenalin content, whether by physiological or chemical methods, it must be borne in mind that the chromaphil tissues not only produce adrenalin but have the capacity of storing it to a certain degree. Changes in the demand of the body for adrenalin may therefore influence the chromaphil tissues in several ways. There may be increased or decreased production of adrenalin with an effect upon the adrenalin load, depending upon the rate at which the adrenalin is given off to the blood. It follows, therefore, that the amount of adrenalin in the suprarenals is not in itself a true index of the activity of these organs. Its determination, however, may give some indication of the amount of production of adrenalin if the animal under experiment remains healthy, and if the adrenalin load be compared with that of a suitable control animal kept under identical conditions. Too much importance, however, must

not be assigned to the adrenalin load of the suprarenals, and its amount must be considered in relation to evidence of increased adrenalin in the blood. The whole question is so much complicated by factors at present unknown, or only partly recognized, that a safe deduction must of necessity be extremely guarded. With these reservations in view the evidence of the effect of hyperthyroidism upon the adrenalin load of the suprarenals may now be considered.

Herring (28) in 1916 found that the suprarenals of thyroid-fed cats, carefully minced and desiccated at 37° C, yielded a material which was more active when tested by Elliott's method (18) on the blood pressure of pithed cats than similarly desiccated suprarenals from the normal animals. By the subsequent employment of the chemical method of measuring adrenalin introduced by Folin, Cannon and Denis (22) Herring showed that the adrenalin content of the suprarenals of male and female cats is considerably increased by the prolonged feeding of these animals with small quantities of raw ox thyroid in addition to their ordinary diet. A histological examination of the suprarenals of the thyroid-fed animal further revealed that the cells of the medulla were closely packed with chromaphil material.

In a later paper Herring (27) extended his observations to albino rats. Male rats of the same age and as far as possible of the same litters, were taken in two groups. One group was fed on small amounts of fresh ox thyroid, the other group was kept as a control and fed with similar amounts of fresh ox flesh, the main bulk of the diet being in both groups a liberal supply of bread and whole milk. The adrenalin content of the suprarenals was estimated by the chemical method. It was ascertained that the amount of adrenalin in the thyroid-fed group was approximately 50 per cent. greater than in the controls. It was further noted that sudden death of the thyroid-fed animals was apt to occur even when the animals were putting on weight and apparently thriving. In all such cases the adrenalin content of the suprarenals was very high, and the condition was associated with a greatly hypertrophied heart and gross changes in other organs. In some of the thyroid-fed rats accessory suprarenals were found to be present and to contain chromaphil tissue in abundance.

In another paper Herring (30) dealt with the effect of thyroid feeding on the adrenalin content of the suprarenals of the female albino rat. It was ascertained that the suprarenals of the female rat normally have an adrenalin content nearly double that of the suprarenals of the male rat of the same size. The female animal is more susceptible to the administration of thyroid than is the male, and reacts in different ways. Some put on weight and remain healthy, and their adrenalin content shows on the whole a slight increase; other animals do not thrive and their adrenalin content falls.

Kuriyama (41) obtained no increase in the adrenalin content of the suprarenals of the albino rat on thyroid feeding. As already mentioned, Kuriyama grouped males and females, his experiments were few, and he employed large doses of desiccated thyroid of unknown activity.

It has been stated by Cramer (11) that external temperature has a considerable effect upon the adrenalin load of the suprarenals. Cold leads to a rapid exhaustion of the adrenalin store. Herring also noted that the mere separation of a litter of young albino rats into different cages adversely affected some of them. Experiments upon adrenalin content must therefore be attended by every precaution against outside influences, and the control animals should be of the same age and sex and preferably of the same litter, kept under conditions identical with those to which the thyroid-fed animals are subjected.

E. R. Hoskins (32) and Herring (29) have demonstrated that small doses of thyroid lead to striking changes in many organs. The hypertrophy of the heart and kidneys is greater than that of the suprarenals.

Kojima (40) and Herring (29) showed that the pancreas is also increased in size, and that this is not a mere matter of congestion is proved by Kojima's description of the numerous mitoses in the nuclei of the pancreatic cells brought about by the administration of small doses of thyroid. Herring came to the conclusion that hyperthyroidism stimulates the production of adrenalin, and that the enlargement of the heart and kidneys is a secondary phenomenon. The simultaneous hypertrophy of the pancreas was interpreted as being compensatory to the disturbance of carbohydrate metabolism associated with increased adrenalin formation. The results, whatever their explanation

may be, lend some support to the theory enunciated in 1908 by Eppinger, Falta and Rudinger (19). These observers as a result of experimental work, and from the consideration of the pathology of certain diseases, more especially myxoedema and exophthalmic goitre, formulated a general scheme whereby the interaction of certain of the ductless glands might be explained. Briefly they regard the glands as obeying the following laws:

I. Extirpation of a blood-gland has a two-fold result. First, a direct action through the loss of its specific secretion. Second, an indirect action through the disturbance of its metabolic relationships with other glands.

II. Between the thyro-parathyroids and pancreas, and between the pancreas and chromaphil tissue, there exists a mutual restraining influence, while between the thyro-parathyroids and chromaphil tissue there is a mutual stimulating influence.

III. Diminution or increase of secretion of one gland leads to over-action or insufficiency of another. For example, hyperthyroidism brings about a relative insufficiency of the pancreas and increased activity of the chromaphil tissue.

The laws enunciated by Eppinger, Falta, and Rudinger cannot be regarded as established, and they are obviously incomplete. They may, however, provide a working hypothesis to be confirmed or altered as experimental evidence dictates. The loss of balance of the ductless glands occasioned by the over- or under-activity of any one of them may ultimately be found to have its origin in changes in metabolism and the production in excess of toxic substances. The work of Noël Paton (55) and his co-workers on the relation of guanidine to tetania parathyreopriva, and of Kendall (38) is very suggestive.

V. The Effect of Hypothyroidism upon the Adrenalin Content of the Suprarenals.

Gley (24) in 1914 found that the suprarenals of dogs and rabbits previously thyroidectomised show no signs of any diminution of their adrenalin content when tested upon blood pressure. Extracts of the suprarenals of parathyroidectomised rabbits were sometimes a little less active than the normal, but in these cases the animals were suffering severely from the effects of the re-

moval of the thyro-parathyroids. Gley saw no trace of any specific action of the thyroids in maintaining the normal content of adrenalin in the suprarenals.

Herring (28) in 1916 noted that the desiccated suprarenals of thyro-parathyroidectomised cats yielded a material which was less active, when tested by Elliott's method on the blood pressure of pithed cats, than was similarly treated material from normal animals. In a further series of animals Herring, using the chemical method of estimating adrenalin, found that the loss of activity occurs only in cats suffering from tetany and obviously ill. In the rabbit, and in cats which show no symptoms, there is no decrease in the amount of adrenalin in the suprarenals. It would seem, therefore, that parathyroidectomy, and not thyroidectomy, is responsible for what loss takes place.

There is no evidence, then, that loss of thyroid in itself occasions any diminution in the amount of adrenalin present in the suprarenals. On the other hand the tetany and wasting which follow removal of the parathyroids are accompanied by loss of adrenalin from the suprarenals.

VI. The Effect of Hyperthyroidism upon the Adrenalin Content of the Blood.

Fraenkel (20) in 1908 attempted to measure the amount of adrenalin in the human blood by a physiological method. He adopted Kehrer's procedure, making the use of the isolated uterus of the virgin rabbit. By noting the response of the uterus to various dilutions of the blood of approximately normal individuals, and comparing the reaction with that produced by known dilutions of adrenalin, he claimed to have demonstrated the presence and measured the amount of adrenalin in human blood. Fraenkel also investigated the blood of individuals suffering from exophthalmic goitre and found in this disease a large increase in the amount of adrenalin. He regarded this increase as a compensatory mechanism on the part of the body against the lowered blood pressure brought about by increased thyroid secretion.

Bröking and Trendelenburg (4) in 1911 repeated the work making use of Laewen's method in preference to Kehrer's. They perfused the blood vessels of the frog's legs with known dilutions of blood serum from normal individuals and from patients

suffering from exophthalmic goitre. The results obtained by the constriction of the blood vessels were compared with those produced by known dilutions of adrenalin. Bröking and Trendelenburg estimated the concentration in normal human blood to be one part of adrenalin in from two to two and a half million parts of blood. In the blood of patients suffering from exophthalmic goitre they found from two to four times this amount of adrenalin.

Krause (42) noted that the enucleated eye of the frog showed dilation of the pupil when placed in the blood serum of patients suffering from exophthalmic goitre, a phenomenon which does not occur when the eye is immersed in the serum of healthy individuals. He also found an increase of adrenalin in the blood of animals previously injected with the juice obtained from the thyroid glands of patients suffering from exophthalmic goitre.

None of this evidence is satisfactory, for, as pointed out by Schafer (59), the physiological tests used for the estimation of adrenalin would also be given by pituitrin. There are other and more serious objections discussed by G. N. Stewart (62). The uterus alone does not furnish a suitable organ for the detection of adrenalin, and is particularly suspectible to the foreign proteins which exist in the blood of a different species of animal.

Stewart urged the necessity of control experiments in which the specific action of adrenalin in causing inhibition as well as contraction was made use of. He selected the rabbit's intestine as being best fitted to show the inhibitory action of adrenalin, and employing these tests in conjunction could find little evidence of the presence of adrenalin in human blood taken from the general circulation. In a later paper Stewart (63), using the same tests, found no evidence of adrenalin in the blood serum of a man suffering from Graves' disease.

The testing of blood for the presence of adrenalin by biological methods is complicated by the fact that a difference in action between blood plasma and blood serum has been alleged. O'Connor (52) believed that the coagulation of blood liberates substances in it having an adrenalin-like action. He found that blood serum causes a greater constriction of the blood vessels of the frog than does a citrated blood plasma. Trendelenburg (67), recognizing this possibility, changed his opinion as to the value

of his previous experiments, and gave a far lower estimate of the amount of adrenalin in the blood. Stewart and Zucker (66) investigated the action of blood plasma and serum under various conditions, and found that the increased action of serum is mainly confined to the blood vessels, and does not affect the uterus and intestine.

Similar objections apply to the use of the eyeball of the frog as a test for the presence of adrenalin in blood. Schultz (60) found it an unreliable method for detecting adrenalin in solutions where the amount present was much greater than could ever be the case with blood.

Ott and Scott (53) obtained an increase of adrenalin in the blood after the intravenous injection of thyroid extract. They made use of strips of the small intestine of the rabbit, the muscle of which responds specifically to adrenalin by loss of tone and inhibition of its rhythmical activity (Magnus, 47). But thyroid is not the only tissue extract which provokes increase of adrenalin in the blood. Ott and Scott found that extracts of parathyroids, pancreas, ovary and other organs have a similar action. Schwartz (61) had previously ascribed the increase of adrenalin after intravenous injection of animal extracts to the action of foreign proteins, and had shown that many substances can exhaust the adrenalin contents of the suprarenals when injected into the blood.

Gley and Quinquaud (25) obtained results similar to those of Ott and Scott. They took the blood from the suprarenal veins of dogs after the intravenous injection of extracts of thyroid and other organs. The blood from the suprarenal vein was then tested on the blood pressure of another dog. It was found that, while extract of thyroid increased the amount of adrenalin in the blood, it was no more active in this respect than extracts of liver and other organs. Gley and Quinquaud prevented the coagulation of the blood by the previous injection into the animal of Witte's peptone or leech extract so as to avoid the objections raised by O'Connor. It is quite possible that the injection of these materials had something to do with their results, for the reactions upon blood pressure which they figure are remarkably uniform in character whatever the nature of the extract used.

It cannot be said that an increase of adrenalin in the blood in hyperthyroidism has been satisfactorily established. Stewart and Rogoff (64) have shown that the amount of adrenalin in the general circulation is extremely small, and they regard its output as being dependent upon the integrity of the nerve supply of the suprarenals. In cats which had the right suprarenal excised and the left semi-lunar ganglion destroyed, the amount of adrenalin present in the circulation was still further reduced. Stewart and Rogoff estimated the amount in the veins of the suprarenals of these animals to be somewhere between 1 part of adrenalin in 300,000,000 and 1 in 700,000,000 parts of blood and in the general circulation to be at least 100 times less than this. The cats, nevertheless, remained healthy, and Stewart and Rogoff came to the conclusion that adrenalin is not indispensable to the body. The weight of evidence accumulated by Stewart and Rogoff is very great, but against it must be placed the fact that some of their results have not been corroborated by other observers whose methods would appear to have been equally careful. Kellaway (37), making use of the paradoxical pupil reaction in cats, found evidence of increased adrenalin secretion in anoxaemia after section of the splanchnic nerves. This did not occur after removal of the suprarenals, or only to so slight an extent as might be occasioned by the action of severe anoxaemia upon the extra-chromaphil tissue. If Kellaway is right, lack of oxygen would seem to have the power of increasing the output of adrenalin by a local action upon the denervated glands. It is quite possible that adrenalin secretion may also be regulated by hormone action. In this connection it is significant that Cannon and McKeen Cattell (7) have shown that the injection of small doses of adrenalin evokes an action current in the thyroids, and that a similar result follows stimulation of the splanchnic nerves, provided the suprarenals have not been previously removed. They further showed that the electrical changes in the thyroid are due to the stimulating action of some material, presumably adrenalin, carried to it in the blood stream from the suprarenals. It remains to be proved if the injection of thyroid can similarly provoke an action current in the denervated suprarenals.

VII. The Sensitizing Action of Thyroid upon Structures Stimulated by Adrenalin.

There is another aspect of the problem which has more experimental evidence in its support and about which there is less difference of opinion, namely, the sensitizing action of the thyroid secretion upon structures which are stimulated by adrenalin.

In 1911 Asher and Flack (2) showed that the thyroids produce an internal secretion which increases the excitability of the depressor nerve of the heart and the pressor effect of adrenalin upon the circulation. Stimulation of the nerves of the thyroid, or the intravenous injection of thyroid extract, greatly augment the activity of response to adrenalin. Stimulation of the thyroid nerves after extirpation of the thyroid has no such effect, and idio-thyrin was also shown to be inactive. Asher and Flack laid stress upon the nervous control of thyroid secretion, and upon the fact that the phenomena of exophthalmic goitre can be ascribed to the action of adrenalin upon structures which have been rendered more sensitive to it by hyperthyroidism.

Further work upon the same subject has been done by Asher (1) and his co-workers. Richardson (57) demonstrated that the isolated heart of the rabbit beats more rapidly and powerfully under the influence of adrenalin when perfused beforehand or simultaneously with extract of thyroid. Shigeshi Kakehi (36) obtained similar results, and found that the heart of an animal which had previously been thyroidectomised shows no difference in this respect from the heart of a normal animal. Levy (43) ascertained that stimulation of the cervical sympathetic nerve in cats augments the pressor action of adrenalin some 200 to 300 per cent, and that this effect does not follow if the thyroids have been removed. He also showed that the iodine-containing compound isolated by Kendall is effective in sensitizing the blood vessels to the action of adrenalin.

Oswald (54) stated that iodo-thyro-globulin increases the excitability of the vagus depressor and splanchnic nerves to faradic stimulation, and that the augmenting effect is in direct proportion to the iodine content of the material employed. Iodo-thyro-globulin from a case of Graves' disease had a similar influence.

Eiger (17), perfusing the blood vessels of the frog, demonstrated that, while extract of thyroid itself has no action upon them, it greatly increases their response to adrenalin. Eiger showed that the blood collected from the veins of the thyroid augments the effect of adrenalin, while that from other blood vessels has no such action. He also found that the blood of rats fed with thyroid, and the blood of patients suffering from exophthalmic goitre, have the same property of increasing the activity of adrenalin.

Santesson (58) claimed that the intravenous injection of various preparations of thyroid increases the sensitiveness of the rabbit to adrenalin. A greater rise of blood pressure is produced by the same dose of adrenalin if the animal is previously fed on thyroid or receives an injection of thyroid extract.

Schafer (59) was unable to confirm the results of Asher and Flack as regards the prior injection of thyroid extract in increasing the excitability of the cardiac vagus or depressor in the rabbit, cat, or dog. He found in the last two animals that the simultaneous injection of thyroid and stimulation of the depressor nerves produce a greater fall of pressure than that occasioned by either of these two alone. The increased depressor effect of the combination he regarded as the result of summation, for in the rabbit, where a slight pressor effect is sometimes produced by the injection of thyroid, the simultaneous injection of thyroid and stimulation of the depressor nerve evokes a smaller response than stimulation of the depressor nerve alone.

Dalmau (15), while believing that the pressor effect of adrenalin is intensified by thyroid, looked upon its action as a mechanical one. He considered that thyroid promotes an absorption of fluid into the blood vessels from the lymph, thereby creating a condition favorable to an increased action of adrenalin.

There is, then, a large amount of evidence that the secretion of the thyroid has a sensitizing action upon the structures stimulated by adrenalin. The reaction is not necessarily a specific one. Kepinow (39) found that the pressor effect of adrenalin upon the circulation is intensified by the preliminary use of pituitrin, and that an augmentation of the reaction of the pupil is obtained in the same way. Cow (10) corroborated Kepinow's statement as regards the blood pressure, and further

showed that pituitrin activates the uterus to an increased response to adrenalin. Cow gave reasons for believing that this sensitizing action of pituitrin is exerted upon the peripheral mechanism of the sympathetic system but not actually upon the end organs. Further research upon these lines is clearly called for.

VIII. The Thyroids and Suprarenals as a Subsidiary Heat-Regulating Mechanism.

Eppinger, Falta, and Rudinger (19) discussed the possibility of adrenalin taking part in the regulation of body temperature. They noted that the injection of adrenalin causes a rise of temperature in normal, thyroidectomised, and depancreatised dogs. On the other hand, towards the close of life in dogs suffering from pancreatic glycosuria a decreased production of adrenalin is accompanied by a gradual fall of body temperature. They concluded that the secretion of adrenalin is an important factor in heat production.

This theory has been developed by Cramer (11) who regards the thyro-adrenal apparatus as a humoral mechanism supplementing the nervous one. Cramer believes that the thyroid hormone mobilises the liver glycogen by increasing the production of adrenalin and sensitising the sympathetic nerve endings. At the same time adrenalin constricts the arterioles of the skin thereby diminishing the loss of heat from the body. Cramer has adduced a number of experimental and pathological observations in support of this theory.

That some mechanism of this kind comes into play as an accessory factor in heat production is not unlikely. The stimulating action of thyroid upon metabolism is well known. Von Noorden (51) stated that "the thyroid acts upon metabolism as a pair of bellows upon a fire." McCarrison (46) said, "the thyroid gland is to the human body what the draught is to the fire." Herring (29) compared the action of the thyroid glands to the draught-regulating mechanism of a furnace.

Increased activity of the thyroid must therefore bring about a greater production of heat. The loss of glycogen from the liver may be simply due to the increased oxidation resulting from hyperthyroidism. The question of the action of adrenalin upon carbohydrate metabolism has received much attention,

and although having a distinct bearing upon the relations of the thyroids to the suprarenals, is far from being settled and is beyond the scope of this article. Even if it be admitted that hyperthyroidism stimulates the suprarenals to an increased production of adrenalin, its action upon other organs is greater. The liver and pancreas would appear to be more intimately concerned. A disturbance of thyroid secretion upsets the balance of many organs, all of which have to be taken into consideration in the interpretation of the picture which ultimately results.

IX. Summary.

There is much evidence, though not unanimous, that hyperthyroidism increases the size and weight of the suprarenals. The observations in this respect are confined to a few species of animals, chiefly the albino rat and it does not follow that a similar change takes place in all animals. In the albino rat the hypertrophy of the suprarenals is due mainly to an increase in the size of the cortex of the gland, the histological features of which have not as yet been investigated. The hypertrophy of the cortex of the suprarenals is associated with gross changes in other organs and in the general metabolism of the animal, and it is to these influences rather than to a specific action of thyroid that the cause may be attributable.

There is some evidence that hyperthyroidism does in the healthy animal increase the adrenalin load of the chromaphil tissues. The adrenalin load, however, is so easily altered by a variety of circumstances that it signifies little in itself. The alleged increase of adrenalin in the blood of animals suffering from hyperthyroidism is neither proved nor disproved. The evidence is untrustworthy. There is greater unanimity in ascribing to the thyroid hormone an activating influence upon the structures which are amenable to adrenalin. This sensitizing action of thyroid may explain the phenomena of Graves' disease which have been attributed to an increase of adrenalin in the blood. It does not exclude the possibility that an increased secretion of adrenalin may actually occur in this condition.

A specific action of thyroid in stimulating the secretion of adrenalin, and in sensitizing the structures amenable to its action, though not improbable is not satisfactorily proved.

Pituitrin has a similar action in sensitizing certain structures to the action of adrenalin, and further experimental work may extend the similarity.

Hypothyroidism is shown to have no effect upon the adrenalin load of the suprarenals, but here again no definite conclusions as to the absence of a specific stimulus can be drawn, for we know nothing about the extent of the requirements of the body for adrenalin in this condition.

The theory that one endocrine gland exercises a specific influence upon another only touches a part of the question. The changes in metabolism which occur when any gland is disturbed in function must have a widely-spread effect. Many of the metabolic changes undoubtedly take place in the liver, and it is unreasonable to suppose that this organ takes no active part in the problems presented by the ductless glands. Hyperthyroidism provokes such gross changes in the organs of the albino rat that one is drawn to look for the explanation of its effects in the products of a disordered metabolism. Noël Paton (56) has emphasized the importance of the endocrine organs as regulators of metabolism. The investigation of the substances normally formed in the body, and the influence which the ductless glands have upon them, provides a line of research which may eventually lead to the establishment of the endocrine glands as important factors in the regulation of the general metabolism of the body.

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THE FIRST CASE OF MYXEDEMA TREATED BY THYROID EXTRACT

To the younger generation of practitioners organotherapy is more or less a commonplace feature of every-day medicine. Its real development, however, has occurred entirely within the lifetime of this generation.

The first successful use of thyroid extract in the treatment of myxedema was begun in 1891 by Dr. G. R. Murray of Manchester, England. The recent death of the subject has impelled Dr. Murray to publish a recapitulation of the case (1).

"Mrs. S., aged 46, was shown at a meeting of the Northumberland and Durham Medical Society on February 12th, 1891. She had had a family of nine children, of whom six were living. At the age of 40 she had a miscarriage, after which she had menstruated once, at the age of 42. When she was 41 or 42 years of age her relations had noticed that she was becoming slow in speech and action, and she herself began to find that it required a great effort to carry on her ordinary housework. The features gradually became enlarged and thickened and the hands and feet increased in size and changed in shape, so that at the time of this meeting she presented the typical features of an advanced case of myxedema of at least four years' duration. After showing the patient, I stated my intention of treating her with thyroid extract, and described the principles upon which this treatment was based and the reasons for expecting that it would be successful. The treatment was not commenced until two months later, and the following note taken on April 13th, 1891, describes her condition at that time:

"She complains of languor, a disinclination to see strangers, and great sensitiveness to cold. The temperature is subnormal, and varies between 95.6° and 97.2° in the mouth. The pulse varies between 60 and 70. The face is blank and expressionless and the features are notably thickened. This change is well seen in the alae nasi and lips. The subcutaneous connective tissue of the eyelids is so swollen that she finds it difficult to look upwards. There is also considerable swelling beneath the eyes and of the cheeks. The hands and feet are both enlarged; the former have that peculiar shape which has been described as spade-like. The skin is very dry, there is no perspiration, and the superficial layers of the epidermis are continually being shed as a fine white powder. The hair is very fine in texture, and a considerable quantity of it has been lost. She is slow in answering questions; all her actions are slow and are performed with difficulty. The speech is remarkably slow and drawling and the memory is bad. No thyroid gland can be felt in the neck. The urine contains no albumin or sugar.

"The experimental nature of the treatment was explained, and the patient, realizing the otherwise hopeless outlook, promptly consented to its trial. In order to insure that the extract was properly prepared, the thyroid gland was removed from a freshly killed sheep with sterilized instruments and conveyed at once in a sterilized bottle to the laboratory, where a glycerin extract was prepared.

"In the treatment of this first case a hypodermic injection of 25 minims of the extract was given twice a week at first, and later on at longer intervals. The patient steadily improved and three months later, on July 13th, the condition was thus described:

"The swelling has gradually diminished, and has practically disappeared from the backs of the hands, the skin over them being now loose and freely movable. The lips are much smaller. The swelling of the upper eyelids has diminished so much that she can look upwards quite easily. The swelling beneath the eyes and of the cheeks has also much diminished. The face consequently, as a whole, has greatly improved in appearance and has much more expression, as many of the natural wrinkles, especially about the forehead, have returned. The speech has become more rapid and fluent, the drawl being scarcely noticeable at the present time. She answers questions much more readily, the mind has become more active, and the memory has improved. She is more active in all her movements, and finds that it requires much less effort than formerly to do her housework. She now walks about the streets without any hesitation, without a companion.

"She has menstruated normally during the last six weeks at the regular interval. For the last four weeks the skin has been much less dry and she perspires when walking. The hair remains as before. She is no longer so sensitive to cold. Unfortunately, owing to circumstances, a daily record of the temperature has not been kept, but out of four observations that have been made lately, about 11 a. m., three times the temperature has been 98.2° F. and once 97.4°.

"After this the injections were given at fortnightly intervals, and later on, when the oral administration had been shown by Dr. E. L. Fox and Dr. Hector Mackenzie to be equally efficient, she took 10 minims by the mouth six nights a week, so that one drachm was consumed in the course of each week. On this dose she remained in good health and free from the signs of myxedema. She continued to take liquid thyroid extract regularly until early in 1918, when it became difficult to obtain, so she was given dry thyroid extract. She enjoyed excellent health until early in 1919, when she died at 74 from cardiac failure.

"This patient was thus enabled, by the regular and continued use of thyroid extract, to live in good health for over twenty-

eight years after she had reached an advanced stage of myxedema. During this period she consumed over nine pints of liquid thyroid extract or its equivalent, prepared from the glands of more than 870 sheep."

1. Murray (G. R.). The life history of the first case of myxedema treated by thyroid extract. Brit. M. J. (Lond.), 1920, (i), 359-360.

ENDOCRINOLOGY IN RETROSPECT AND PROSPECT

With this issue ENDOCRINOLOGY completes its fourth year of publication. While the retrospections of a four-year-old may not be regarded as highly portentous, something of value may be deduced from the consideration of even this brief experience.

The declared central purpose in the organization of the Association for the Study of Internal Secretions was "to correlate the work and interests of physicians and students engaged in the study of internal secretions and, by concerted effort, to broaden knowledge in this field." The constant aim of the editorial staff has been to coöperate to the best of its ability in the realization of this aim.

Starting with no resources but an idea and the enthusiasm of its proponents, it was expected that progress would in any case be somewhat slow. Almost as soon as the journal got under way, however, it had to encounter the vicissitudes of war. A large proportion of the active men upon whose support reliance was placed either entered directly into military service or assumed such heavy duties in connection with the war that little time and energy were available for the Association and its journal. That the infant survived this trying ordeal seems a surprising manifestation of innate vitality.

Not only, however, was the preoccupation of its supporters a handicap to the Journal, but the disorganization of medical and scientific activities throughout the world also proved a seriously disturbing factor. The supply of original articles for publication was reduced almost to the vanishing point and the periodical literature from which abstracts are derived became difficult to secure. Many journals suspended

publication and those which continued publication in many cases reached the abstracters only irregularly. In fact, many library files are still incomplete for the period of the war. Partly on this account, hundreds of articles published in the past three years remain yet to be abstracted.

Three plans for dealing with the current literature have been entertained. The first of these is to collect the literature in abstract form, as it appears. The publication of this material affords a cross section of the literature for the given period. If adequately presented, such a cross section should exhibit in a colorless way both the virtues and defects of this literature. That various palpable absurdities have thus been presented for the consideration of the readers is fully realized.

As regards articles of dubious value, the policy of most abstract journals is to pass them over without notice, in the hope of their relapsing promptly into oblivion. In the meanwhile, however, the titles have been catalogued in the more complete bibliographic journals and they remain, to the thorough student, at least, a factor that must be taken into account. For example, an author proposes to bring up to date the literature on a given point. From the bibliographic journals he secures a list of references to all sorts and conditions of articles. Frequently none of these can be discarded without at least cursory consideration. If the articles were all available in adequate abstract form, those of no permanent value could at once be dismissed from consideration. For this reason, it is felt that the re-publication of even so-called trash is of constructive value. Accordingly, the policy is to abstract "all the endocrine literature since 1916."

Not the least of the difficulties encountered in carrying out this plan resides in the scientific conscience of the abstracters. In each case the aim has been to secure the services of men of well-balanced critical judgment. Such men have a readily understood hesitancy to attach their initials to material of dubious significance, even as reporters.

So much for the first plan. It represents to a considerable extent merely a preliminary process.

A second plan is to collect the literature on given topics, irrespective of date, and to publish this material as a series

of synthetic reviews, in which each article is critically evaluated by a competent authority. Only a beginning has been made toward the evolution of this plan. It amounts to a presentation of the literature—to carry out the morphological simile—in reconstruction.

A third plan is to collect in abstract form and publish in chronological sequence the literature on select topics—to present this literature in longitudinal section. Obviously, the literature on some topics, for example, Graves' disease, would not lend itself to such treatment. That on other and less extensive topics might, however, be thus presented and a great deal of work be saved upon the part of those having occasion to review such material. So far it has not been practicable to proceed with this plan.

A fourth plan, also, namely, to supply translations or abstracts of less accessible individual articles to our members and subscribers, has had to remain one for future development.

At this time it may not be amiss to point out that the limiting factor is solely the elementary one, an inadequate budget. One of the leading scientific societies is said to expend approximately $50,000 a year upon its abstract journal alone. The actual realization of the maximum possibilities for usefulness in an abstract and bibliographic service might exhaust an even larger budget. There is readily accessible the most complete collection of the current literature on medicine and medical sciences in the world. Translators and abstracters are also obtainable. Salaries alone are lacking.

A rapidly growing subscription list is an encouraging indication of the future possibility of augmenting the usefulness of the Association and its journal. The time, however, would seem to have arrived when, in recognition of their place as educational institutions, associations and journals of this sort should be supported by considerable endowments. When the needs and possibilities of such are realized and adequately presented, doubtless such endowment will be forthcoming.

So much for the matter of second-hand dealings with the literature. As regards original material, the endeavor has

been and will be to publish at first hand a considerable proportion of the best articles appearing in the field of Endocrinology. Articles of wide interest and such as summarize the results of extensive studies are especially to be desired. The coöperation of the entire membership of the Association is needed to make the most of this phase of our activities.

With the beginning of Volume V, the Journal will appear bimonthly. The material to be presented is constantly increasing in amount, and bimonthly issues will perhaps be of more convenient size than would quarterly. It is hoped that this consideration, together with that of more prompt publication of original articles and abstracts, will compensate for the additional effort and financial outlay involved.—R. G. H.

LE SYMPATHIQUE ET LES SYSTEMES ASSOCIES. By A. C. Guillaume, with preface by Pierre Marie, Paris, 1920. Masson et Cie., 160 p.

In view of the close relationships between the autonomic nervous system and the endocrine functions this book will be of interest to endocrinologists generally. In addition to introductory and concluding sections the volume consists of six chapters, taking up, respectively, the morphophysiologic conception of the autonomic system, the connection of this system with the organic processes, the pharmacologic relationships, the syndromes due to selective excitation of the system, clinical "vagatonia" and "sympathicotonia" and the pathological connections of the autonomics with the "organic" and "animal" systems. The morphologic relationships are brought out in a series of unusually comprehensible diagrams. In the section on pharmacology the author goes, in the interest of philosophical gratification, considerably beyond the limits of safety. He postulates a function for the suprarenal cortex bearing the same relation to the parasympathetic system as does the medulla of the gland to the sympathetics. "Hormone x" in this case is cholin. The pancreatic secretion is alleged to have a somewhat similar function to that of the suprarenal cholin. He also oversimplifies the equasion in assigning to the thyroid hormone merely a selective affinity for the sympathetic fibres rather than regarding it as a general cell stimulant. On the whole, the book, while illuminating and full of useful data, must be read somewhat critically. The data are largely derived from other compilations.—R. G. H.

BEITRAEGE AM SCHILDDRUESENFRAGE (THE GOITER PROBLEM). By Otto Bayard. Basel, 1919. Benno Schwabe & Co., 42 p.

The author likens goiter to beriberi, in that both may develop when patients go from one country to another, owing to differences of food encountered. He considers goiter as a deficiency disease, iodine being the lacking factor. Especially during youth the organism needs a large amount of iodine. The less iodine in the food the larger is the thyroid. In Kiel, situated at the seaside, the average thyroid is smaller than in Berlin. In Berlin it is smaller than in Munich. The size of the gland in Bern is larger than in Munich. The greater the distance from the sea, the larger the size of the thyroid.

The iodine has to be fixed in the cells of the body and the author believes (though why is a mystery) that it is fixed only in the nucleus. He applies Ehrlich's side-chair theory of anti-

toxin formation to the thyroid problem. In youth the cells have more receptors for thyrjod (the name the author gives to the active principle of the thyroid) than in advanced age. Therefore, during life the cells gradually lose these thyroid receptors. When the function of the thyroid is diminished there will be too small an amount of thyroid to saturate all receptors and some receptors which do not get saturated, disappear. When this happens during youth the cells come to have only the number of receptors that they otherwise have in more advanced years. Therefore . . . cretins have an oldish face and make an oldish impression. This conception, to the reviewer, seems downright fantastic.

As a prophylaxis against goiter the author recommends that the public be restricted from using salt for cooking except such as has been supplemented with potassium iodide (5-10 mg. to 5 k. of salt).

On the whole the book, while full of original ideas, contains so many unproved assertions as to demand a highly critical attitude upon the part of the reader.—J. K.

(IL PROBLEMA DELLA SONNO. LE AZIONI ORMONISCHE REGOLATRICI DEL FENOMENO.) SLEEP AND ITS HORMONE REGULATION. By Prof. Mario Barbara. Palermo, 1920. Scuola Tip. Boccone del povero. 39 p. 8°.

The author postulates as the essential feature in sleep an alternation of anabolic and catabolic predominance due in turn to alternately preponderating activity of "excito-anabolic" and "excito-catabolic" hormones. The problem as previously regarded is thus translated into newer phraseology.—R. G. H.

DIE REIZTHEORIE UND DIE MODERNEN BEHANDLUNGSMETHODEN DES DIABETES. By Priv. Doz R. Kolisch, Berlin and Vienna, 1918. Urban und Schwarzenberg, 152 p.

The question whether diabetes is caused by increased formative or diminished oxidation of sugar has given rise to an enormous literature. Claude Bernard was the first who considered increased formation as the cause. In Germany this theory was not accepted and well known specialists like Külz, von Noorden and Minkowski wrote against it. Kolisch was one of the first authors in Germany to support in his "Reiztheorie," the view of Claude Bernard. "Diabetes is caused by increased formation of sugar in the tissues. This is due to abnormal stimuli; these stimuli may be toxic or nervous." Though in the begin-

ning this theory received little credence, modern research has more and more supported it.

In this little book Kolisch describes his theory and discusses the literature pertaining to it. The best treatment is to try to diminish the abnormal stimuli by rest. Therefore, it is necessary to give as little food as possible to the patient, and not only to restrict the carbohydrates but also the protein. The influence of opium on glucosuria is very clear, considered from this point of view: it diminishes the irritability of the overstimulated nerves.

It is unfortunate that the author has written the last five pages of this book, wherein he discusses the Allen treatment in a way to indicate that he scarcely knows even the most fundamental things about it. Except for this last chapter the book is excellent and may be warmly recommended to those interested in the history of research in the field of diabetes.

Some figures quoted from the mortality statistics of Vienna are used by Kolisch as evidence of the value of under-nourishment in the prevention of death from diabetes.

DEATHS FROM DIABETES IN VIENNA, AND TOTAL MORTALITY

	Total Mortality		Cause of Death: Diabetes	
Year	Civilian	Military	Civilian	Military
1913	32,130	184	337	2
1914	31,480	1,788	292	2
1915	33,052	3,966	265	6
1916	33,494	4,137	265	15
1917	40,260	5,871	194	15

—J. K.

ABSTRACTS

ADRENAL insufficiency and war (L'insuffisance surrénale et la guerre). Agnel (E.), Thèse de Paris, 1918-19, **143.**

The importance of adrenal insufficiency in the pathology of war is discussed by Agnel. Its chief causes are overwork, wounds and infections of various kinds, of which the most important are dysentery, malaria, tuberculosis and various intoxications, such as food poisoning, alcoholism, chloroform, arsenobenzol, antityphoid and cholera inoculation and gas poisoning.—Med. Sc. Abst. & Rev., **2,** 133.

(ADRENAL) Recovery from Addison's disease. Anon. Lancet (London), 1920, **(i),** 923.

This editorial is devoted to the description of a case of Addison's disease ending in recovery. It was described by Giraudeau in his inaugural thesis (Paris, 1919-20, No. 31). Death occurred from cancer of the stomach eleven years later, when the autopsy findings confirmed the original diagnosis. Scar tissue was found in the right suprarenal, indicating the occurrence of inflammation many years previously. The nature of the lesion could not be determined. There was no evidence of tuberculosis or syphilis in the other organs. The case was treated with suprarenal extract for about six months, during which time all symptoms disappeared. Therefore Giraudeau concludes that in cases in which generalized and transient suprarenal incompetence is the result of a localized inflammatory lesion treatment may be effective, whereas it is of no avail in caseous tuberculosis of the suprarenals.—L. G. K.

ADRENAL extract as emergency medication in Erb's myasthenia during severe attacks (L'extrait surrénal total, médication d'urgence dans la myasthenie de Erb an cours des accidents graves). Marie (P.) & Bouttier (H.), Bull. et. mem. soc. Méd d. hôp. (Paris), 1920, 3. s., **44,** 575-581.

Report of a case of Erb-Goldflamm's myasthenia improved by the intramuscular administration of extracts of the whole adrenal gland.—F. S. H.

ADRENALS, Note on the development of — in the hedgehog (Note sur les développement de la surrénale du béris-

son). Célestino da Costa (A.) Compt. rend. Soc. de biol. (Paris), 1920, **83,** 878-879.

Of embryological interest.—T. C. B.

Grave ADRENAL insufficiency during influenza (Dos casos de insuficiencia suprarrenal grave durante la gripe). Clemente (M.), Siglo Med. (Madrid), 1919, **66,** 1057-1060.

Two cases are described. The suprarenal insufficiency was indicated by marked asthenia, vomiting, diarrhea, small pulse, extreme hypotension, lividity of the nose and extremities, Sergent's white line—in short, a syndrome amounting precisely to collapse with retention of the mental faculties. Energetic treatment with adrenalin by mouth and hypodermatically resulted favorably. [The abstractor has noted in various fatal cases of this type in the Hospital Gral at Madrid, that the adrenals were the site of well-marked lesions.]—G. M.

(ADRENAL) Addison's disease in a girl of thirteen years, death, autopsy (Maladie d'Addison chez une fille de treize ans, mort, autopsie). Comby (J.), Arch. de Méd. d. Enf. (Paris), 1917, **20,** 28.

Report of a characteristic case with caseation of both adrenals. Of interest because of the age.—C. H. G.

(ADRENAL) Association of a marked pigmentation and lichenous growth on the buccal mucosa during the course of an evasive adrenal insufficiency (Association d'une pigmentation considérable et d'un lichen de la muqueuse buccale au cours d'une insuffisance surrénale fruste). Crouzon & Bouttier, Bull. et mem. Soc. d. med. hôp. (Paris, 1920, 3. s., **44,** 67-71.

A detailed case history unamenable to abstracting.
—F. S. H.

(ADRENALS) Treatment of tuberculosis with adrenochrom (Adrenochrombehandlung der Tuberkulose). Diesing, Deutsche med. Wchnschr. (Berlin), 1920, **46,** 598-599.

Adrenochrom is an extract from adrenals, made with alcohol, ether and benzine and containing adrenalin, sulphur and phosphorus. It is injected in doses of 0.2-0.5 cc. of 1:1000 solution. Adrenaline dilates the pulmonary vessels; sulphur diminishes the amount of oxygen in the lungs; phosphorus increases the formation of connective tissue. The author saw

splendid results in tuberculosis of the lungs and recommends it also in surgicul tuberculosis.

[No histories of patients are reported; the article gives the impression of an advertisement rather than a report of serious pharmacological work.]—J. K.

ADRENAL-vascular syndrome (El sindrome suprarreno-vascular). Duran, La Clinica Contemporánea, 1918, ——, ——. Symptomalogical description without significant data. —E. B.

(ADRENAL) Chemical and morphological studies of cholesterin and cholesterin esters in normal and pathologically altered organs (Chemische und morphologische Studien über das Cholesterin und Cholesterinester in normalen und pathologische veränderten Organen). Fex (J.), Biochem. Ztschr. (Berlin), 1920, **104**, 82-174.

The free and combined cholesterin varies but slightly from the normal in the liver or kidneys in various pathological conditions. The free cholesterin of the adrenals shows no significant variations from the normal but the combined cholesterin esters vary greatly. These variations are attributed to a normal physiological fluctuation rather than to a pathological increase.—F. S. H.

ADRENAL apoplexy in small children (Nebennierenapoplexie bei kleinen Kindern). Friederichsen (C.), Jahrb. f. Kinderh. (Berlin), 1918, **87**, 109.

Friederichsen emphasizes the importance of adrenal hemorrhage and consequent acute adrenal insufficiency in the study of adrenal function and pathology. He reports two cases of patients, aged 3 and 10 months, respectively, and cites twenty-eight more from an extensive review of the literature. The majority of the cases occur in well developed, previously healthy children under one year of age. The onset is acute, with a cry and often with vomiting. There is a rapid development of cyanosis and pallor without dyspnea or pulmonary symptoms. The temperature is high, 39-41° C. The pulse is small, feeble and very irregular. Physical examination shows a normal heart and lungs. Cyanosis of the extremities rapidly appears and several hours after the onset and shortly before exitus it is replaced by a purpuric efflorescence. This begins as numerous dusky red petechiae, which rapidly spread and become confluent if not well nigh universal. Exitus occurs

six to twenty-four hours after the onset. Post-morten examination shows cutaneous and adrenal hemorrhages. The primary cause of the adrenal hemorrhage is unknown, though the author states that the acute onset and fever suggest an overwhelming infection. The clinical picture is similar to that following adrenal extirpation in animals, and the author believes it to be determined by an acute adrenal insufficiency. The purpura is secondary to this latter, perhaps as a result of a loss of peripheral vascular tone with consequent stasis. The author draws an interesting analogy between the purpura and the bronzing in Morbus Addisoni. The prognosis is determined by the degree of disturbance of adrenal function and two cases are cited in which old adrenal hemorrhage was found at autopsy. Adrenalin therapy is indicated.—C. H. G.

(ADRENAL) Case of malignant adrenal cortex tumor with metastasis in the liver (Ein Fall von maligner Nebennierenmarkgeschwulst mit diffuser Metastase der Leber). Fujimori (Yuhei), Verhandl. d. japan. path, Gesellsch. (Tokyo), 1916, **6,** 187.

An autopsy report. The subject was a woman of 35. The metastatic growth had completely infiltrated the liver, which was enlarged to a weight of 745 grams.—R. G. H.

(ADRENALS) Plethysmographic exploration of the blood circulation in the suprarenal capsule (Exploration plethysmographique de la circulation sanguine dans la capsule surrénale. Hallion (L.), Compt. rend. Soc. de biol. (Paris), 1920, **83,** 335-336.

Description of a plethysmograph for studying the circulation in the adrenals.

(ADRENAL) A case of congenital sympathetic neuroblastoma combined with Addison's disease in a child (Ein Fall von Neuroblastoma sympaticum congenitum, combiniert mit Morbus Addisonii bei einem Kinde). Hertz (P.) & Secher (K.), Jahrb. f. Kinderh. (Berlin), 1918, **87,** 367, 1pl.

A case report with a record of complete clinical and pathological findings.—C. H. G.

(ADRENALS) The functional connection between the suprarenal cortex and other glands of internal secretion, in white rats. Hewer (Evelyn E.), J. Physiol. (Lond.), Proceedings 1920, **53,** xcvii-xcviii.

A preliminary communication. Both feeding and inoculation experiments are being carried on. The work is not complete.—T. C. B.

(ADRENAL) On the suprarenal glands in congenital syphilis. Jubo (M.), Verhandl. d. jap. path. Gesellsch. (Tokyo), 1919, —, 59.

The author concludes that there must be some relation between congenital syphilis and status thymicolymphaticus since in both cases similar alterations are found in the suprarenals, which are characterized chiefly by hypertrophy of the cortex and incomplete development of the medulla.—E. V. C.

The ADRENALS and pathology of war (Les glandes surrénales en pathologie de guerre). Loeper (M.) & Oppenheim (R.), Rev. gén. de path. de guerre (Paris), 1916-17, **1**, 123-141.

A somewhat extensive review of the voluminous French literature on the etiologic and therapeutic aspects of the suprarenal glands. The authors believe that the glands play an important role in muscular fatigue, exhaustion, and in the reactions to traumatism, infectious diseases, specific vaccinations, toxins and poisons. In short, one gathers that, in the minds of the authors, bodily weakness and adrenal deficiency are approximately interchangeable terms. In accordance with this conception, adrenal medication is extensively indicated. In more severe cases adrenin in doses of 3-4 mg. hypodermically or intravenously is recommended. In less severe cases adrenalin, 20-40 drops daily, by mouth, is advocated. Glycerine extracts of adrenal substance administered hypodermatically, are said to be remarkably efficacious in grave infections. In delayed convalescence, asthenia and chronic depression desiccated adrenal substance is used. It is reported that adrenal opotherapy has been largely employed among soldiers in accordance with the foregoing principles and much service thereby rendered.—R. G. H.

(ADRENAL) The so-called post-mortem suprarenal softening. Materna (A.), Arch. f. path. Anat. etc., (Berl.), 1920, **227**, 235-265.

Mild grades of central softening are commonly found in the adrenals. Most often it is associated with acute infections such as sepsis, pneumonia and intestinal inflammations. There is increase in weight, lymphocytic infiltration, hemorrhages,

edema and necrosis. In the cortex there is frequently pigmentary degeneration and rapid disappearance of lipoidal material.—Chem. Abst. **14**, 2023.

ADRENAL cortex tumor in a woman with virilism (Tumeur de la couche corticale de la capsule surrénale droite observée chez une femme et ayant provoqué l'habitus masculin). Mauclaire (P.), Bull. et Mem. Soc. de Chir. de Paris, 1920, ——, —— (May 25); Abst., Arch. méd. Belges, **73**, 263.

Mauclaire adds another case of virilism of suprarenal origin to those recorded in the literature by Appert, Launois, Auvray and Tuffier, Quinby, Thumin, Glynn and others. Mauclaire's case was that of a woman of 38, who, for the previous six years had noted the development of a tumor of the abdomen. During this time her menses became suppressed and her facial appearance altered to a masculine type. Her body, neck and chest became covered with hair. Her breasts atrophied and the feminine, rounded form of the body was transformed to the muscular male type. At operation a tumor was found in relation with the inner border of the right kidney. Histological examination showed it to be of suprarenal origin.
—R. G. H.

(ADRENAL) Pigmentation of the limbus corneae in Addison's disease (Über Pigmentation des Limbus Corneae bei Morbus Addisonii). Meesmann, Deutsche Med. Wchnschr. (Berlin), 1920, **46**, 644.

Demonstration of a case of Addison's disease in which there were not only the well-known pigmentations of the conjunctivae but also a closed ring of pigment on the limbus corneae. The pigment was situated in the middle and deep layers of epithelium. The walls of the lymph vessels were filled with pigment.—J. K.

ADRENAL insufficiency following the injection of novarsenobenzol in recurrent fever. Remarkable effects of adrenalin in this and another case, showing syndrome of toxic hemiparesis of like origin (Insuffisance surrénale aigue consecutive a l'injection de novarsénobenzol dans la fièvre récurrente. Effets remarquables de l'adrénaline dans ce cas, ainsi que dans un syndrome d'hémiparésie toxique de même origine). Monziols & Collignon, Bull. et mem. Soc. med. d. Hôp. (Paris), 1920, 3. s., **44**, 214-215.

The administration of 1 mgm. adrenaline is systematically followed out by the authors to counteract the symptoms

of adrenal insufficiency after the giving of 0.3 grams novarsenobenzol for recurrent fever. Uniformly favorable results are reported. The case of hemiparesis was similarly cured by the injection of 3 mgm. adrenaline the first day and 1 mgm. on each of the three succeeding days. The cause of the adrenal insufficiency is attributed to the rapid destruction of the spirochetes by the arsenical treatment and the resultant liberation of a large amount of toxins. These overpower the adrenals so that their detoxicating function can not operate to an adequate extent and symptoms of insufficiency result. Adrenalin is assumed to tide the patient over this period until his suprarenals are again able to cope with the conditions.

—F. S. H.

ADRENAL changes in experimental scurvy (Uber die pathologischen Veränderungen der Nebennieren bei experimenteller Barlowscher Krankheit nebst Gewichten einiger endokrinen Drüsen bei derselben). Morikawa (Y.), Osaka Igakkwai, 1920, **19**, 9.

The author has found the following changes in the suprarenals in experimental Barlow's disease in guinea pigs: (1) Increase in weight, (2) Increase in lipoidal content of the cortex, (3) Reduction in amount of doubly refractile fat, (4) Distribution of the lipoid in the zona fasiculata in three layers —an outer rich in lipoid, a middle poor in lipoid and an inner rich in lipoid. He concludes that this hypertrophy, which is similar to that found in polyneuritis gallinarum, indicates that the absence of a necessary vitamine is also an etiological factor in Barlow's disease.—E. V. C.

ADRENALS, Development of—in man (Considérations sur les capsules surrénales ou cours du développement chez l'homme). Mutel, Compt. rend. Soc. de biol. (Paris), 1920, **83**, 357-360.

An embryological and anatomical consideration of the causes of variation in the right and left glands. Non-proportional growth, fixity of the vascular pedicle and displacement of the neighboring organs are the three causes of the variation.—T. C. B.

ADRENALS, The smooth muscle fibers of the central vein of the— (Les fibres musculaire lisses de la veine centrale surrénale). Peindarie (J.), Compt. rend. Soc. de biol. (Paris), 1920, **83**, 958-960.

Description of a system of smooth muscle fibers connected with the central vein of the suprarenal and its principal affluants. The author thinks these muscular formations play an important role in the physiology of the gland. Emotive adrenal discharge appears to be only the result of general vaso-constriction of the veins, collectors of the secretion, which are compressed and emptied of their contents. This is said to invalidate the seductive hypothesis of Cannon.—T. C. B.

(ADRENAL?) Premature sexual development. Phillips (J.) & Lambright (G. L.), Arch. Ped. (N. Y.), 1920, **37**, 282.

The authors report a case of a girl seven years old who was 4 feet, 4 inches tall and weighed 73½ pounds. She gave a history of having been a robust child who developed unusually large breasts at the age of two years, pubic hair at five with well developed genitals. Between the ages of three and four years she was seized with convulsive attacks which gradually increased in severity; these resembled epilepsy, being ushered in with a cry, followed by clonic and tonic contractures of the right side of the face and extremities. Menstruation was established with an increase in the severity and frequency of these attacks. Examination showed a premature sexual development in that she presented pubic hair, axillary hair, breasts and broad pelvis, all of normal adult size. Her mentality was below par. The bones of the right side of the face and the femur were large. The authors give a short resume of the literature on the subject. No tumor was noted. X-ray examination of the skull and the sugar tolerance test were both negative. Because of the negative skull picture the negative sugar tolerance test and the absence of any definite pituitary or pineal pressure symptoms, the authors by exclusion take the case to be one of involvement of the adrenal cortex.

—M. B. G.

ADRENAL insufficiency, influenza and manic-depressive psychoses (Grippe, insuficiencia suprarrenal y psicosis maniacodepresiva). Rossi (Santín C.), Anales Fac. de Med. (Montevideo), 1919, **4**, 801-812.

Nine cases are reported in which manic-depressive psychoses developed during the weakness following influenza. The weakness was interpreted as indicating suprarenal deficiency. Similar evidence of the same sort was noted in cases of six other manic-depressives who had not had influenza. Adrenalin treatment proved beneficial, i. e., the patients' condition improved while they were receiving the drug. On this

basis a far-reaching theory is elaborated to the effect that the data reported lift the veil of mystery from this type of psychosis, indicate the etiology and point out the therapeusis.
—R. G. H.

(ADRENAL THYROID) Influenza as a pulmonary necrotic alveolitis involving the endocrines. Sajous (C. E. de M.), N. Y. Med J. (N. Y.), 1920, **111**, 837-846.

The Pfeifer bacillus upon reaching the alveoli of the lungs finds all suitable conditions for growth and develops colonies which arrest the function and cause necrosis of the alveoli. The alveolar lesions interfere with the respiratory processes of the system at large, thus causing asphyxia of all organs, including the adrenals, whose hormone enables the hemaglobin to be converted to oxyhemaglobin and sustains the tone of the arterioles. The thyroid exerts powerful influences on the general metabolism and its secretion and iodine are physiological constituents of an active factor in the systemic defense against infections which acts by sensitizing pathogenic bacteria to phagocytosis. It also facilitates the proteolytic activity of the enzymes, which serve to destroy or, rather, digest, bacteria. Hence, prophylaxis against influenza may be established by the inhalation of iodine fumes, by therapeutic doses of strychnine, which excites the adrenals, and by thyroid gland to increase general opsonic and phagocytic activity. The active treatment of influenza consists of absolute rest, calomel and salines, deep inhalation of iodine fumes and salicylates. When the temperature is down strychnine and adrenal preparations may be freely given.—H. W.

(ADRENAL-GONAD) Early development of the secondary sex characters in a two-year-old girl following a hypernephroma of the right kidney (Frühzeitige Entwicklung der sekund. Geschlechtecharaktere bei einem zweijahrigen Mädchen infolge einer Hypernephroms der rechten Nebenniere). Schiff (E.), Jahrb. f. Kinderh. (Berlin), 1918, **87**, 519.

A clinical and pathological case report. The child was adipose, with marked hypertrichosis, the pubic hair being especially well developed. The breasts were normal. The sella was slightly enlarged. The histological examination showed the endocrine organs to be normal. Clinical differentiation from Frölich's syndrome was simple owing to the palpable abdominal tumor.—C. H. G.

ADRENIN, Pathological physiology of— (Contribucion al estudio fisiopatolojico de la adrenalina). Sepúlveda V (H.), Innaug. Dissertation, Santiago de Chili, 1917.

To determine the concentration of adrenin in the blood the author used the following technique: To 4 or 5 cc. of a 5 per cent solution of mercuric nitrate in N/10 silver nitrate in a tube graduated in small units blood serum is added drop by drop until there is complete precipitation. This requires 1 to 2 cc. of serum. The mercury salt forms a white gelatinous and the silver, a whilte caseous precipitate. This is filtered off. The filtrate is transparent or slightly opaque. To this is added, drop by drop, standardized permanganate solution until a light rose coloration is produced. By this technique the author determined a maximum value of 0.30 gms. per mil. of adrenin in normal adults. Determinations were made on ten subjects who were not fatigued. In subjects who were ill the quantity of adrenin averaged in general less than 0.30 gms. per mil. The determinations appeared to have considerable prognostic value. With findings of less than 0.12 gms. the prognosis is very grave; from 0.12 to 0.20, it is doubtful; above 0.20, the majority of the patients recovered.—J. R. P.

(ADRENIN) On the permeability of the placenta for adrenalin in the pregnant rabbit and albino rat. Shimidzu (Yoshitaka), Am. J. Physiol. (Balt.), 1920, **52,** 377-394.

In multiparous animals there may be several fetuses of both sexes in one uterus; one pregnant animal, therefore, incloses several hormone systems. In deciduate animals these systems are separated by the placenta, and the question arises whether the placenta is permeable to these hormones. The aim of the present experiment is to learn whether adrenalin administered to a pregnant animal will increase the adrenalin in the fetus. Rabbits and albino rats were used. The conclusion is that the placenta is impermeable to adrenalin, to the extent at least, that we cannot increase the adrenalin of the fetal blood by subcutaneous injections of the drug into the mother.—T. C. B.

(ADRENIN) Essentials in measuring epinephrin output, with further observations on its relation to the rate of the denervated heart. Stewart (G. N.) & Rogoff (J. M.), Am. J. Physiol. (Balt.), 1920, **52,** 521-561.

A further reply to Cannon with protocols of experiments and a full discussion of the results. The paper should be read

in the original for numerous details. It is contended that the acceleration of the denervated heart by asphyxia cannot be taken as an index of increased epinephrin output; it may be obtained and may not be diminished after the adrenal veins have been ligated, after complete isolation of the adrenals from the circulation, and after complete removal of the adrenals. When it does not occur it is due to deterioration of the animal. There is no good evidence that asphyxia causes augmentation of epinephrin output by a direct action on the cells of the adrenal medulla. Opening of the abdomen does not interfere with the acceleration caused by asphyxia. The catheter method of estimating changes in the rate of epinephrin output is defective in principle. It can only measure changes in concentration. The fundamentally correct method is to collect the blood and assay it.—T. C. B.

(ADRENIN) The relation of the epinephrin output of the adrenals to changes in the rate of the denervated heart. Stewart (G. N.) & Rogoff (J. M.), Am. J. Physiol. (Balt.), 1920, **52,** 304-363.

A lengthy article in which the authors describe experiments showing that acceleration of the denervated heart is not a reaction by which the rate of epinephrin output can be measured. Clipping off the adrenal vein has no effect on the heart reaction caused by sciatic stimulation, although it markedly diminishes or abolishes reactions which are known to be genuine reactions to epinephrin. Acceleration of the denervated heart on sciatic stimulation is well obtained in cats which have had one adrenal removed and the nerves of the other sectioned, and also when both adrenals have been removed. The reaction is well obtained after opening the abdomen as in the operation for a cava pocket. When the reaction disappears after the removal of the adrenals it is not because of the absence of increased epinephrin discharge on stimulation of the sciatic, but for other reasons, such as deterioration of the animal which interferes with the reflexes involved in the reaction or with the capacity of the heart to accelerate its beat.
—T. C. B.

ADRENALIN and guanidin. Preliminary communication. Burns (D.) & Watson (A.), J. Physiol. (Lond.), Proceedings, 1920, **53,** xcix-c.

In the course of investigation on the action of guanidin on the neuro-muscular mechanism of mammals the adrenalin blood pressure reaction was used as a measure of sympathetic

irritability. The injection of 1 cc. of 1.7 per cent guanidin hydrochloride into the jugular vein of the cat produced no effect on the carotid pressure. Three minutes later 1 cc. of 1/1000 adrenalin caused a slightly supranormal rise of pressure which was sustained for at least double the normal time. A nerve-muscle preparation was subjected to a bath of 1/100,000 adrenalin, then 0.02 per cent guanidin hydrochloride, and again to adrenalin. On stimulation with a minimum break shock the contraction was supranormal in extent, duration and rapidity of onset. The guinea pig's uterus showed similar effects.—T. C. B.

(ADRENIN PITUITRIN) Experimental studies on the effect of anesthetics in shock. Cattell (McKeen), Am. J. Surg. (N. Y.), 1920, **34**, 89-91.

As an incidental part of the work, the effects of adrenin on the heart of animals in shock under ether anesthesia, were studied. After an overdose of ether certain animals were resuscitated by adrenin. It was found that this resulted in a marked lessening of the sensitiveness to ether, due to an influence exerted apparently on the heart, since stimulation of the peripheral blood vessels with pituitrin produced no such decrease of sensitiveness to the anesthetic.—R. G. H.

(ADRENIN) Attempt at poisoning by adrenaline (Tentative d'empoissonnement par la solution a adrenaline 1/1000°). Grasset (R.), Bull. et mem. Soc. med. d. hôp. (Paris), 1920, 3. s., **44**, 981-985.

The attempt to commit suicide by drinking 15 grams of adrenaline solution (1:1000) proved abortive, although two hours or more elapsed between time of the ingestion of the drug and medical treatment.—F. S. H.

Influence of ADRENIN on heat regulation (Über die Wirkung der Adrenalins auf die Warmeregulation). Kondo (S.), Acta Scholae Med. Univ. Imp. in Kioto, 1919, **3**, 169-205.

The author finds that adrenalin only brings about an increase in body temperature when it is administered in large amounts either subcutaneously, intravenously or intraperitoneally, and further, that when the vagi are treated with atropin or are sectioned this increase in temperature is inhibited. He is of the opinion that these observations indicate the existence of a double innervation: a sympathetic poisoned by adrenalin and a parasympathetic poisoned by atrophin.

Intra-cerebral injection of adrenalin increases the temperature only slightly after thyroid extirpation.—E. V. C.

ADRENIN medication in the persistent vomiting of pregnancy. (Vomissements incoercibles de la grossesse et médication adrénalique). Rathery (F.) & Bordet (F.), Bull. et mem. Soc. med. d. hôp. (Paris), 1920, 3. s., **44**, 778-784.

A report of a case of persistent vomiting in pregnancy of two months, during which the patient suffered from inanition and dehydration, accompanied by acidosis. After two or three days of treatment by injections of adrenaline in large amounts of normal saline, the symptoms ceased and did not reappear when the drug was withdrawn. The rapidity of the action of the drug is to be noted. The doses used were: First day, 0.5 mgm. subcutaneously; second day, 1 mgm. subcutaneously and 1 mgm. ingested; third day, same dose; fourth day and following seven days, 1 mgm. ingested. The increase in weight was very rapid and at the rate of one kilo per day for nine days. The medication used was not the extract but adrenaline; it did not cause glycosuria.—F. S. H.

ADRENIN, The behavior of the blood pressure curve after—injection in children with various pulse qualities (Über das Verhalten der Blutdruckkurve nach Adrenalininjektionen bei Kindern mit verschiedener Pulsqualität). Schiff (E. R.) & Epstein (B.), Jahrb. f. Kinderh. (Berlin), 1920, **91**, 128.

The authors found that children with normal pulse quality react to adrenalin with a marked blood pressure increase. On changing from the upright to the horizontal posture the blood pressure is unchanged. Pale children with pulse of poor volume and tension but without appreciable vaso-lability react with a minimal blood pressure increase or none at all. On lying down the blood pressure increases 20-30 cm. of water. Pale children with pulse of poor tension and volume, with apparent vaso-lability, show a prompt but very slight blood pressure increase and no change upon standing or lying down. The response found in the latter two groups is rather uncritically ascribed to a functional inferiority of the vascular system leading to a defective response to stimulation of the vasomotor innervation.—C. H. G.

(ADRENIN) Circulatory disturbances in the acro-contractures. Direct muscular adrenalinization and electric reactions (Troubles circulatoires dans les acro-contractures. Adrénalization musculaire directe et réactions électiques).

Sicard, Roger & Simom. Bull. et mem. Soc. med. d. hôp. (Paris), 1917, 3. s., **41**, 811-814.

The injection of adrenalin directly into the living muscle substance results in fibrillary contractions and hyperexcitability to both mechanical and electrical stimulation.—F. S. H.

A case of general, absolute ALOPECIA of emotional origin (Un caso di alopecia generale assoluta do origine emotiva). Todde (Carlo), Riforma med. (Napoli), 1920, **36**, 382-383.

The A. reports a case of a soldier of 34 who had previously been wounded and then released from the service in Italy, only to be called again to the colors and sent to France, where he had to stand a week of bombardment from airplanes. After this trying period he began to lose his hair, at first from the exposed parts, afterwards from the whole body. He had never before had any infection or skin disease except phlectenular conjunctivitis, but was of lymphatic constitution. The family history indicated hereditary nervous taint and the subject presented certain symptoms suggesting exophthalmic goiter. His case was accordingly classified as an endocrine disturbance and he was put under treatment of pluriglandular therapy. Boschi has reported the case of a woman whose hair dropped out after severe emotional stress but reappeared under thyroid treatment.—G. V.

AMAUROTIC FAMILY IDIOCY, or infantile amaurotic idiocy. Epstein (J.), Med. Rec. (N. Y.), 1920, **97**, 224-227.

Epstein reports five cases of this unusual disease. "It may not be impossible that the much wanted etiology will ultimately be found in some abnormal action or reaction in the endocrine group which has a profound influence over the general metabolism and the life history of the nerve cells. But, at present, there is no evidence of an endocrine pathology in infantile amaurotic idiocy."—H. L.

Endocrine factors in bronchial ASTHMA (Endokrinen Grundlagen des Bronchialasthmas). Curschmann (H.), Deutsch. Arch. f. klin. Med. (Leipzig), 1920, **132**, 362-378.

Asthma may be related to and caused by endocrine disturbances, though medical men rarely think of this fact. The author observed two cases of intermittent Graves' disease. Each time the symptoms reappeared the patient had attacks of asthma. That there exist relations between asthma and the parathyroids is well known. Attacks of asthma with symp-

toms of tetany (so-called broncho-tetany) have been repeatedly described. These cases are cured by calcium, which is a specificum against tetany. Whether the adrenals are related with asthma is not known. Real asthma during Addison's disease has never been described. Hyperfunction of the adrenals is only observed as sympathicotonia in Graves' disease. In these cases asthma has never been observed. The ovaries have an influence as is proved by the asthma beginning in the menopause. The author describes one case (which does not prove much.—J. K.). In another case asthma regularly returned during menstruation. Relations between asthma and the testicles are not known. It is possible that the hypophysis has an influence. A case is described in which diabetes insipidus and asthma developed at the same time. Post-mortem examination disclosed a tumor of the mediastinum with metastasis in both adrenals, hypophysis, lungs, kidneys and spleen. The author believes that these facts may prove of great importance in relation to treatment. In cases in which asthma begins in the menopause, the ovary should be treated. When there is hypothyroidism, thyroid may be given also. Curschmann has seen no good results with hypophysis medication in asthma, though it has been recommended by Borchhard.
—J. K.

CAROTID GLAND, Adenoma of the— Reid (M. R.), Johns Hopkins Hosp. Bull. (Balt.), 1920, **31**, 177-185.

Not of immediate endocrine interest.—R. G. H.

CORPUS LUTEUM in neurological practice. Climenko (H.), N. York M. J. (N. Y.), 1918, **109**, 302-305.

See Endocrin., **3**, 1-15.

CORPUS LUTEUM, The nausea and vomiting of pregnancy. Davis (C. H.), Wisconsin M. J. (Milwaukee), 1920, **18**, 513-518.

No beneficial results followed the administration of corpus luteum in cases that gave a history of ovarian insufficiency and abortions.—H. W.

(CORPUS LUTEUM) Experimental histological studies on the origin of the corpus luteum. Hirose (T.), Tokyo Igakkwai, 1920, **34** (No. 2).

Mention is first made of the two conflicting theories regarding the origin of the lutein body. According to the first

(Sabotta), the lutein cells arise from the granulosa; while according to the second (Johann), they become differentiated from the cells of the theca interna. The author used the following criteria for differentiating between the corpus lutein cells and the theca lutein cells: (1) Relation to the connective tissue, (2) location in reference to the hyaline limiting membrane, and (3) fate of the granulosa cells. He used as material the ovaries of 16 rabbits taken from 5 hours to 21 days after copulation, and of 10 pregnant and 16 non-pregnant women. He concluded that the lutein cells of the corpus luteum and the interstitial cells arise from the cells of the theca interna. The paper is well illustrated and a good deal of literature is reviewed.—E. V. C.

(CORPUS LUTEUM) War amenorrhea (Über Kriegsamenorrhöe). Köhler (H.), Zentralbl. f. Gyn. (Kiel), 1919, **43,** 359-368.

A clinical report of four cases of amenorrhea in which microscopic examination of the ovaries led the author to the conclusion that the "war amenorrheas" are primarily due to disturbances of nutrition which in turn cause a lack of functioning of the corpus luteum.—F. S. H.

(CORPUS LUTEUM) Preservation of the procreative function in women. Langstroth (F. W.), N. Y. Med. J. (N. Y.), 1920, **111,** 982-986.

Langstroth cites an instance of a woman who suffered one or two severe headaches each month, similar headaches following the administration of corpus luteum preparations. The author believes this subject had an anaphylactic reaction to her own corpus luteum secretion. Extensive surgical repair work was done but the headaches continued.—H. W.

CORPUS LUTEUM extract in vomiting of pregnancy. Quigley (J. K.), N. Y. State J. M., 1919, **19,** 306.

Data reported elsewhere. See Endocrin., **4,** 115.

The DUCTLESS GLANDS and constitutional diagnosis. Gutman (Joseph), Med. Rec. (N. Y.), 1920, **97,** 558-561.

"In the interpretation of a case from the constitutional standpoint several fundamental facts concerning the functions of the ductless glands upon which the study of human constitutions is based must be borne in mind: (1) The effect of the

inherited powers of the endocrine system upon the development of the individual; (2) their control of all metabolic processes of fundamental importance; (3) their domination of all vital functions occurring during the three cycles of life; (4) their co-operative method of functioning and intimate relationship, and (5) the consequences resulting from a derangement of their functions or of glandular dyshormonism." Gutman agrees with Fraenkel's classification of endocrine constitutions: the thyrotrope, adrenotrope and pituitotrope, and the mixed types. The subject in case of each type is peculiar in build, height, skin, hair, mental capacity, character, ambition and predisposition to certain diseases. "Whether an individual is to be tall or short, lean or corpulent, graceful or awkward is all dependent upon the peculiar reaction of the different glands individually and collectively." The author believes the cardiovascular, gastrointestinal, vasomotor, respiratory, sexual and other systems fully subservient to the glandular hormones. According to Gutman every functional expression is not an accident but a corollary of endocrine expression.—H. L.

Further development of an interesting case of ERB-GOLDFLAM'S DISEASE and remarks on the nature of this disease (Ulteriore decorso di un interessante caso di morbo di Erb-Goldflame ealcune considerazioni sulla natura di questa malattia). Capezzuoli (Cesare), Riv. crit. di clin. med. (Firenze), 1920, **21**, 97-114.

After a detailed report of a case the author insists on the desirability of further study of this disease on the basis of endocrine dysfunction (pluriglandular), as it seems justified from the frequent accompanying lesions of the thymus, of the thyroid, hypophysis and parathyroids. Its being found often mixed with other endocrine syndromes as well as its familiar type and the usual determining causes give a new weight to his hypothesis. In other words, he considers the syndrome as an individual idosynerasy to abnormal products of endocrine dysfunction, sufficient to bring about the disease in hypersensitive subjects.—G. V.

(DWARFISM) The metabolism of a dwarf. Talbot (F. B.), J. Am. M. Ass. (Chicago), 1920, **74**, 1225.

A basal metabolism study of a dwarf boy. He was seven years of age, weighed, clothed, 12.6 K. (normal weight for boy of seven years is 21.9 K.) and was 91.5 cm. in height (normal, 114.3 cm.) The author found that the total metabolism for

twenty-four hours was 780 calories as compared with an average of 900 calories for a normal boy of the same age. This is almost within the normal limits of variation. When the total calories for twenty-four hours were compared with those of boys of the same weight, it was found that he was producing more than the average (780 against 675). This is slightly above the possible variations from the normal. When his metabolism was considered from the viewpoint of unit of body weight, it was found to deviate markedly from the normal. His calories showed an increase of 45 per cent (58 calories per Kgm. against 40 for a normal boy of the same age) and his metabolism per Kgm. of body weight, an increase of 13.7 per cent above the normal. His metabolism per unit of body surface was 12 per cent higher than that of normal boys of the same age and 11 per cent higher than that of normal boys of the same weight. There was no clinical evidence of any disturbance of the glands of internal secretion.—F. C. P.

(DIABETES) Experiments on carbohydrate metabolism and diabetes. I. Intravenous glucose tolerance of dogs. Allen (F. M.) & Wishart (M. B.), J. Biol. Chem. (Balt.), 1920, **42**, 415-458.

The paper forms the first of a series concerning the endocrin function of the pancreas. The results reported are generally in harmony with those of other workers and demonstrate that in dogs rendered diabetic or near-diabetic by partial depancreatization there occurs a reduction of sugar tolerance, although marked exceptions occur. Extensive tables are given in lieu of protocols.—F. S. H.

Experiments on carbohydrate metabolism and DIABETES. II. The renal threshold for sugar and some factors modifying it. Allen (F. M.) & Wishart (M. B.), J. Biol. Chem. (Balt.), 1920, **43**, 129-147.

Extensive experiments on dogs, either completely or partially depancreatized, demonstrate that a diminished renal permeability for glucose in the sense of a raised threshold is definitely proved as the rule in diabetic animals. As the same rule holds for the great majority of human diabetics, this demonstration furnishes one more point of similarity between the experimental and clinical conditions. Various possible causes for the elevation of the threshold are discussed. The prolonged excess of sugar in the blood may be an important factor, but some considerations seem to oppose it. Certain observations suggest that high fat diets may raise the sugar

threshold in diabetes even without acidosis. The renal function may be affected by various extraneous causes, of which the elevation of the threshold by epinephrine is one interesting example. No interrelation of the renal and pancreatic functions is demonstrable in the sense of an increased readiness of sugar excretion even in totally depancreatized animals. An elevation of the threshold seems to be connected particularly with severity of the diabetes, but a teleological interpretation of this as a protective mechanism for saving sugar to the body is considered dubious—F. S. H.

(DIABETES) Estimations of sugar in the blood in the diagnosis and treatment of diabetes. Cammidge (J. P.), Practitioner (Lond.), 1920, **104**, 114-130.

The author describes the methods of Lewis and Benedict, Folin and Wu, and his own for estimating quantitively the sugar in the blood. He emphasizes the range in sugar values which lie within normal limits, 0.06 to 0.14 per cent, and how such variations depend upon the nature of the food and the time after a meal the determination is made. The blood sugar curve in diabetes is similar in form to the normal, but it has a wider time relation and attains a greater height as a rule. In severe cases a permanent hyperglycaemia is established and the percentage of sugar in the blood never drops within normal limits, even after a night's fast. In a normal person the difference between the percentage of sugar in the blood two hours after the sugar has been swallowed and when fasting should not exceed 0.01 per cent. A study of over 700 cases of diabetes induces the author to believe that there is no constant blood-sugar level for the appearance of sugar in the urine in quantities recognizable by ordinary test; and also that there is no definite relationship between the percentage of sugar in the blood and either the percentage or total amount of sugar excreted by the kidneys. Hyperglycaemia may exist without glycosuria and is sometimes the cause of boils, carbuncles, sciatica. Patients with a permanently high blood sugar may pass comparatively little sugar in their urine, while, in some instances, a normal, or even a subnormal, blood sugar curve may be associated with frank glycosuria. In either condition, examination of the urine alone does not give a correct picture of the case, and, if it is not checked by blood sugar estimations under controlled conditions, may readily lead to mistakes in diagnosis and treatment. As a rule, young diabetics have a lower threshold point for clinical glycosuria than those of middle age, and the threshold rises with advancing

years. It is, therefore, important that the presence of even small amounts of sugar in the urine of persons of middle age should not be dismissed as of little significance, unless a series of blood tests have shown that their tolerance for carbohydrates is not seriously defective. Hyperglycaemia may exist without clinical glycosuria, that is with an insufficient percentage of sugar in the urine to give the ordinary tests for sugar. The reverse condition, glycosuria with a normal or subnormal percentage of sugar in the blood, is not as uncommon as is generally supposed. Twenty-five per cent of obese people have hyperglycaemia without glycosuria. Cases of glycosuria with normal blood sugar are either examples of latent diabetes or renal diabetes. The former group, Cammidge believes hepatic in origin; the latter, a congenital abnormality depending upon abnormal permeability of the kidneys for sugar. He reports a unique instance of renal diabetes in father and daughter. He considers a low blood sugar content in ordinary diabetes as a good sign even when a large amount of sugar is being passed in the urine. Such patients become sugar free more rapidly and ultimately acquire a comparatively high tolerance. He believes that hyperglycaemia even without glycosuria is more readily controlled if the fat content of the diet is materially reduced. He writes: "Permanent success in the treatment of diabetes can only be secured by keeping the blood sugar curve within normal limits, even though more severe restriction of the diet may be necessary to attain this end than is required to keep the urine sugar free." He considers a high blood sugar level with no glycosuria more serious than a low blood sugar level with moderate glycosuria. Hyperglycaemia occurs in other conditions than diabetes. In nephritis its presence is a serious omen and indicates a speedy termination. High blood sugar curves are frequently encountered in carcinoma and hyperthyroidism.

—H. L.

(DIABETES) The prevention and treatment of diabetic coma. Cammidge (P. J.), Lancet (London), 1919, **(i)**, 60-64.

The author maintains that acidosis can no longer be accepted as the sole cause of diabetic coma, but that it is often an associated or merely an incidental phenomenon. The failure of alkali therapy has been one of the main stumbling-blocks in the way of a general acceptance of the acid intoxication theory. Coma is rather to be considered as the consequence of auto-intoxication, but the available evidence suggests that it is a toxemia resulting from the general failure of metabolism occurring in diabetes, instead of from a specific toxin

originating in a break in the chemistry of the body in one particular direction. It is likely that coma is produced by several toxins of different origin acting together. Probably toxic substances resulting from abnormal protein metabolism are responsible for a part of the symptomatology of diabetic coma. A deficiency of inorganic salts may also be a factor. In order, therefore, to prevent coma the diet must be arranged in such a way that: (1) The patient's tolerance for carbohydrate, fat and protein is not exceeded; (2) the total load of food is within his metabolic capacity; (3) the diet is correctly balanced; (4) a sufficient supply of inorganic salts is provided. If coma has already developed absolute, rest in bed is essential. The bowels should be cleared by enemata. The diet should consist of 2 ounces of lemon juice and 7 to 8 ounces of potato or 2½ to 3 ounces of oatmeal taken in the form of gruel, in small quantities, at 3 to 4 hourly intervals over the 24 hours. As much liquid as possible should be administered. If speedy improvement does not occur alkaline injections should be tried. Massive doses, controlled by repeated examinations of the blood or by estimations of the alveolar CO_2 are necessary. Cardiac stimulants are advisable at an early stage.—L. G. K.

Syphilitic DIABETES due to sclero-gummatous pancreatitis (Diabète syphilitique par pancréatite scléro-gommeuse). Carnot (P.) & Harvier (P.), Bull. et mem. Soc. med. de hôp. (Paris), 1920, 3. s., **44.** 71-76.

Clinical and post-mortem report of a case of diabetes in a syphilitic due to gummous lesions of the pancreas. The subject, a woman of 53, had shown symptoms of neurosyphilis and diabetes for about two years. The urine had been abundant and had contained from 66 to 72 gms. of sugar per liter. Death was due to pneumonia. The pancreas was found to be transformed almost entirely into a sclerogummatous mass. The authors regard this as the first reported case of diabetic manifestations due unquestionably to syphilitic lesions of the pancreas. Four other cases from the literature are cited but in these autopsy showed only ordinary sclerosis of the pancreas.
—F. S. H.

DIABETES A Roentgenologic study of the gastro-intestinal tract in—; a report of seventy-two cases. Case (James T.), J. Am. M. Ass. (Chicago), 1916, **67,** 858-861.

Case found that in diabetes gall bladder involvement is very common. The stomach empties with unusual rapidity.

Duodenal stasis is rare but illiac and low grade colonic stasis is very common.—R. G. H.

(DIABETES) The amount of tissue hydration in diabetes mellitus (Le taux d'hydration des organes dans le diabete sucré). Chauffard (A.), Brian (Mille. P.) & Jacobs (J.), Bull. et mem. Soc. med. de hôp. de Par., 1918, 3. s., **42**, 49-51.

From a comparison of the water content of the tissues of a normal (?) individual with the tissues of one dying in diabetic coma and one having diabetes but dying of tuberculosis, the authors are of the opinion that among diabetics it is only those dying in coma who give evidence of tissue dehydration as the result of the pathological processes. [See also Chauffard, Endocrin., **4**, 144.]—F. S. H.

DIABETES MELLITUS, The limitation of starvation in ——. Edgar (T. W.), N. Y. Med. J. (N. Y.), 1920, **111**, 803-806.

Starvation of diabetics will cause a loss of sugar in the urine, but at the same time it results in the production of acidosis and ketonuria. The prevention of acidosis, therefore, is the logical treatment of this disease. This is accomplished by alkinization and a diet sufficient to maintain weight. The Edgar serum which "contains the internal secretion in hormone form" is capable of increasing the carbohydrate tolerance of certain cases from 25 to 60 per cent and arrest the progress of the disease. The serum is obtained from rabbits after they have undergone a series of maneuvers calculated to activate the various endocrine organs to augmented activity.—H. W.

(HYPOPHYSIS) Diabetes insipidus after meningitis serosa (Diabetes insipidus in Anschlusz an Meningitis serosa). Foerster (A.), München. med. Wchnschr., 1920, **67**, 694-696.

Report of a case. Subcutaneous injection of extract of the posterior lobe of the hypophysis gave temporary improvement. The most active drug is pituitin; less action was seen from pituglandol. Hypophyisin had no effect whatever.—J. K.

(DIABETES) Transitory glycosuria of renal type. The relation between renal diabetes, phlorizin-glycosuria and diabetes mellitus (Transitorische Glykosuria mit renalem Typus. Das Verhältnis des renalen Diabetes zur Phlorizin Glykosurie und zum Diabetes mellitus). Galambos (A.), Deutsche med. Wchnschr. (Berlin), 1920, **46**, 600-602.

No new facts. A case is reported of a young man with a transitory renal glycosuria. The amount of carbohydrates ingested had no influence on the glycosuria. The amount of blood sugar was normal. Only when glycose was given or phloridzin was injected was the quantity of sugar in blood and urine increased for a short time. It is sometimes very difficult to differentiate renal glycosuria from ordinary diabetes. The author observed a case of classical renal glycosuria with acidosis.—J. K.

(DIABETES) Epileptic attacks during diabetes with acidosis (Crises épileptiques au cours d'un diabète avec acidose). Guillain (G.), Bull. et mem. Soc. med. de hôp. (Paris), 1920, 3 s., **44,** 808-810, Abst., Prog. Méd. (Paris), 1920, **35,** 302.

A case report. The case is reported of a patient who, during the course of two months, developed acute diabetes with polyuria, polydipsia, polyphagia and emaciation. During this time he suffered numerous epileptic attacks with left hemiparesis, the crises coinciding with marked acetonuria. The convulsive attacks were highly characteristic, with contracture, biting the tongue and incontinence of urine. They ceased after several days' intensive alkaline treatment; at the same time the hemiplegia receded. This hemiplegia was no doubt of toxic cortical origin. The Babinski sign was consistently negative.—R. G. H.

The history of DIABETES mellitus. Horwitz (P.), N. Y. Med. J. (N. Y.), 1920, **111,** 807-812.

An interesting survey of the history of diabetes mellitus.
—H. W.

DIABETES, Advantages of class instruction in the treatment of—. Janney (N. W.), N. Y. Med. J. (N. Y.), 1920, **111,** 806-807.

The treatment of diabetes should consist of immediate attention and the education of the patient to appreciate his condition and care for himself. Where possible, classes of instruction are of decided benefit in the handling of such cases.—H. W.

DIABETES and exopthalmic goiter (Diabète et goitre exopthalmique). Labbé (M.), Bull. et mem. Soc. med. d. hôp. (Paris), 1919, 3 s., **43,** 955-962.

The non-fortuitous coincidence of diabetes and exopthalmic goiter is well brought out by the author's description and discussion of 5 cases in which the two disorders occurred in the same individual. In one of his cases the woman developed goiter at 20; glycosuria became installed at 50, and at 54 the symptoms of severe exopthalmic goiter developed and the diabetes became aggravated. Each time there was a hyperthyroid attack, with tachycardia, the sugar content of the urine and blood ran up high, scarcely modified by dietetic measures, but subsiding with the paroxysm of hyperthyroidism. He cites Manby, Lancereaux and others' reports of instances of diabetes in some members of a family and exophthalmic goiter in others. All types of diabetes apparently may occur with exophthalmic goiter, but in general they seem to be more resistant to treatment than do the ordinary uncomplicated cases. Hereditary influences seem to play a part and the disorder easily runs into an acidotic condition which may be associated with the disturbed nitrogen metabolism of the goitrous. Therapeutically the medicaments, such as quinine and salicylate, which act against the goiter, also retard the glycosuria. In two of the cases cited iodine treatment was successful; at the same time that the palpitations and tachycardia subsided, the glycosuria also decreased. Labbé is of the opinion that the diabetes of Basedow's disease is probably the result of a functional disturbance of the thyroid.—F. S. H.

(DIABETES) L'épilepsie acidosique. Labbé (M.), Bull. et mem. Soc. med. d. hôp. (Paris), 1920, 3. s., **44**, 810-811; Paris Méd., 1920, **10**, 354-358.

Report of 4 cases of diabetes in which epileptic seizures occurred accompanied by acidosis, together with a discussion of the literature. Labbé concludes that diabetic epilepsy is a manifestation of acidosis. In cases of acidosis in which there is no cause for assuming uremia or any other intoxication, occasionally epileptiform seizures develop which it seems justifiable to associate with acid intoxication. They are localized or general, and are followed by loss of consciousness, either transitory or prolonged. They may precede diabetic coma, or appear after the diabetic coma has begun, or occur long before coma sets in.—F. S. H.

Experimental pancreatic DIABETES after partial pancreatectomy. Langfeldt (E.), Acta Med. Scand. (Stockholm), 1920, **53**, 1-192.

This number of the journal is devoted exclusively to an account of Langfeldt's two years of researches on the develop-

ment of glycosuria in dogs of different ages after partial pancreas ablation. In order to make the metabolism of the animals more like the human metabolism, the dogs were fed on carbohydrates without meat for a long period of time before the operations. Four dogs, prepared in this way, were operated upon. The tolerance for carbohydrates was tested, giving glucose by mouth; normal dogs of the same litter served as control animals. Two of the dogs were operated, when 3-4 months old, 8/9 and 7/8 of the pancreas, respectively, being removed. For 3 months after the operations the tolerance decreased; then it increased and reached that of the control animals. Six to eight months later the tolerance gradually decreased and the dogs developed chronic diabetes. When 8/9 of the pancreas was removed in a fully grown dog, glycosuria developed immediately after the operation. In the last dog operated on as a puppy, 6/7 of the pancreas was removed. The tolerance was repeatedly tested; it was not decreased until one year after the operation. Different portions of the pancreas were removed in different cases, but with no change in results. The chronic diabetes of the dogs showed close resemblance to the human type, the symptoms being polydipsia, polyuria, loss of weight, ketonuria, albuminuria and cataract. The D:N ratio was relatively high and the nitrogen excretion in hunger, low. The ketonuria reached a considerable degree. The diabetic dogs died 8 and 13 months, respectively, after the operations, while the others were killed when the tolerance decreased. In the diabetic dogs no islands of Langerhans were found at autopsy, but they were intact in the animals without spontaneous glycosuria. The findings thus confirm the preponderance of the pancreas in all diabetic phenomena. It appears to have a catalytic action. When the sugar content in the blood reached a higher level than 0.19 per cent, glycosuria followed. Duration of the high sugar content was of greater import than higher concentrations for shorter periods. The article is in English. The autopsy findings are illustrated by 12 photomicrographs. A bibliography of 167 titles is included.—K. M.

DIABETES, The relation between creatinuria and acidosis in—(Forholdet mellem Kreatinuri og Acidose ved Sukkersygen). Lauritzen (M.), Ugesk. f. Læger, (Copenhagen), 1919, **81**, 1595-1605.

After a résumé of the literature of this subject and a description of the technique he has adopted, Lauritzen gives details of several cases of diabetes illustrated with charts, in

which he analyzed the daily excretion of nitrogen, creatin, and ammonia. The first case showed that the excretion of creatin followed a curve parallel with that of the excretion of ammonia. Only during two "hunger days" did these two curves fail to run parallel. This parallelism of the creatinuria and ammonia excretion was also observed in several other cases. In one case the acetonuria and diaceturia were greatest when the creatinuria was at its highest. Lauritzen suggests that the curves of creatinuria and ammonia excretion ran parallel because the diabetic diet affected acidosis and creatinuria in the same way. When, in slight cases of diabetes, creatinuria appears before acetonuria, this, he suggests, shows that restriction of carbohydrates in the diet leads to creatinuria more readily than to acetonuria. He believes that there is insufficient evidence for assuming that acidosis per se leads to creatinuria in diabetes. It is more probable that faulty carbohydrate metabolism is the common cause of both these conditions. He dismisses as untenable the hypothesis that the creatinuria of diabetes is due to incomplete conversion of creatin to creatinin, with consequent excretion of creatin in the urine.

Probably the demonstration of creatinuria before the development of acetonuria will prove of little value in connexion with the early diagnosis of a pre-comatose state, for its onset is indicated by symptoms easier to gauge than creatinuria. But it may be of benefit to the diabetic that creatinuria is combated, for if it is protracted it may contribute to weakness of the muscular system. And, as these investigations show, creatinuria can be controlled by the same dietetic treatment that reduces acidosis. The degree of creatinuria is of prognostic significance: if it is considerable and continuous, it is of bad omen.—Med. Sc. Abst. & Rev., **2**, 296.

DIABETES, coma as a cause of death in ——. McCay (D.), and others. Indian J. Med. Research (Calcutta), 1919, **7**, 22-80.

The absence of acidosis during the course of the treatment of diabetes and even in terminal coma indicates that coma as a terminal phenomenon in diabetes as found in India is unlike European diabetic coma. It is probably uremic. McCay gives evidence that without true nephritis, simple albuminuria may lead to fatal uremia. For comparison blood analyses of 25 normals were made. In 10 walking cases of simple glucosuria without albuminuria somewhat higher values were found for non-protein N (N. P. N.), urea and the ratio N. P. N.:total N.

In 45 cases of albuminuria without glucosuria and 26 cases of albuminuria with glucosuria a retention of urea or other N. P. N. and an increase in the N. P. N.:total N. ratio were found. Blood phosphates were normal and but slight changes occurred in blood alkalinity, as determined by Wright's method, in 71 cases but anti-diabetic treatment (milk and green vegetables) assisted in the elimination of N-waste products. In 25 cases of uremia and severe kidney involvement there is a still greater retention of N. P. N. with or without increase in urea. The N. P. N.:total N ratio in severe cases was from 1:5 to 1:15. A retention of phosphates and a decrease in blood alkalinity were also observed in severe cases. In uremia of chorea, anuria from whatever cause, and eclampsia, the retention of N. P. N., urea and phosphates and the decrease in alkalinity were marked. Acetone was found in the urine and blood of some cases but not of others just as ill. In 13 cases in the terminal stages of diabetes as seen in India, diacetic acid and acetone were generally absent. Positive results of other workers using the $FeCl_3$ test are due to the alkaline condition of some urines. Acidosis and diabetic coma practically do not occur in India, but the terminal coma in India is uremic and not diabetic. The fundamental derangement of the kidneys that accompanies diabetes is the important factor leading to coma and death. Typical "air hunger" is never found among natives. Two cases of diabetes among Europeans had "air hunger" and acidosis.—Chem. Abstr., **14**, 2368.

The treatment of DIABETES in India. McCay (D.) and others, Indian J. Med. Research (Calcutta), 1919, **7**, 81-147.

The incidence of diabetes among the indolent well fed classes; its comparative rarity among working classes; and the fact that meat-eating Mohammedans living under otherwise identical conditions with the Hindu, escapes, while his indolent, sugar-sodden companion develops the disease, all point to causative influence exerted by the ill effects of a prolonged and excessive, one-sided carbohydrate dietary. There is an apparently close association between the one-sided carbohydrate type of diet and decreased HCl of the gastric juice, fermentative dyspepsia, oxaluria or renal calculus, hyperphosphaturia and glucosuria. The oxaluria is a sign of gastro-intestinal catarrh that often precedes glucosuria. The evidence points to a slow atrophy of the pancreas. The authors confirm the fact that extracts of liver and trypsinogen lessen the excretion of sugar for short periods, and found the rice, soy bean and oatmeal cures worthless. In hundreds of cases

they found no starvation period necessary, and in Indian diabetes could always clear up the sugar excretion and lower the blood sugar by removal of carbohydrates from the diet. Patients rarely die from diabetes as found in India and it seldom passes into the graver forms of the disease. Reduction of the carbohydrate intake is practically never followed by severe acidosis. A trace of acetone may occur in the urine; diacetic acid was never found in thousands of analyses; the NH_3 of the urine remains constant.—Chem. Abst., **14,** 2369.

Treatment of DIABETES with caramel (Beiträge zur Behandlung von Diabetikern mit Karamel). Reimer (Georg), Deutsches Arch. f. klin. Med. (Leipzig), 1920, **132,** 219-240.

Caramel is very useful in the treatment of diabetes; it has a caloric value, it does almost never produce glucosuria and it diminishes acidosis. Some persons cannot take it, however, because they get diarrhea. It has an especially good influence in young patients. It should be taken over a period of several days, 100-200 grams daily in coffee, pudding or alcohol. Vegetables and fat may be given at the same time. It is better not to give other carbohydrates or proteins on caramel days.

—J. K.

DIABETES, The importance of renal function in —— (Die Bedeutung der Nierenfunktion in der Zuckerkrankheit). Schirokauer (H.), Deutsche med. Wchnschr. (Berlin), 1920, **46,** 791-793.

It is a well known fact that hyperglycemia can exist without glycosuria when the kidneys are not permeable to sugar. Von Noorden has written that often when a diabetic develops Bright's disease the glycosuria disappears and the diabetes is cured. This is, of course, not true. Diabetes is not glycosuria. Glycosuria is only one of the symptoms of the disease. On the other hand, an increased amount of blood sugar without glycosuria may occur without diabetes in cases of chronic nephritis with increased blood pressure. In cases of hypertension without pathological changes in the kidney the blood sugar may be increased also. All glands of internal secretion have an influence on carbohydrate metabolism. Perhaps the kidney itself has an internal secretion. The author cites some experiments from the literature to support this view. Hence it is possible that the kidney has an influence on sugar metabolism. It will be necessary to include in experimental and clinical work on diabetes a study of the changes in the kidneys

and of the influence of the kidneys on carbohydrate metabolism.—J. K.

DIABETES und syphilis. Simmonds, München. med. Wchnschr. 1920, **627**, 734.

The author made postmortem examinations in 300 cases of diabetes. In 20 cases syphilis was found, but only in 3 did there exist syphilitic changes of the pancreas.—J. K.

The drugless therapy of DIABETES. Stark (H. S.), N. Y. Med. J. (N. Y.), 1920, **111**, 800-803.

The use of opiates and drugs in general is condemned in the treatment of diabetes. Endocrine gland therapy is useless; their failure to remove or alleviate the symptoms is the best possible argument to disprove the influence of internal secretions in the causation of the disease. A consideration of dietary measures is given for the treatment of diabetes.—H. W.

(DIABETES) Coma diabeticum during pregnancy (Ueber Coma diabeticum bei Schwangeren). Umber (F.), Deutsche med. Wchnschr. (Berlin), 1920, **46**, 761-763.

Patients with diabetes very rarely become pregnant. The author describes two cases of women in whom the diabetic symptoms regularly increased during menstruation. Both died in coma during the fourth month of pregnancy. No abortion took place. In a third case a woman with diabetes innocens became pregnant and died in the sixth month, in coma. In this case the woman during coma was delivered by caesarian section of a child that lived less than 24 hours. The blood sugar percentage of the mother during coma was 0.437, and that of the child only 0.091 per cent. [Carlson has found that in partially pancreatectomized animals glycosuria may be in abeyance during pregnancy and the animals kept in fairly good health, but succumb to diabetes after parturition].—J. K.

(DIABETES) The treatment of a mild case of diabetes mellitus. Woodyatt (R. T.), J. Missouri State M. Ass. (St. Louis), 1920, **17**, 227.

A practical talk at a meeting of the St. Louis Medical Society, stressing the importance of the educational phase in the treatment of diabetic patients in securing the best average of results in a large number of cases of all classes and illustrating a specific manner of teaching a patient of the dispensary class.—Author's Abst.

(ENDOCRINE FUNCTION TESTS) Some results of glandular tests made according to the previous condition of the endocrine functions (Quelques résultats des épreuves glandulaires suivant l'état antérieur des fonctions endocriniennes). Claude (H.) & Bernard (Suzanne), Bull. et mem. Soc. med. d hôp. (Paris), 1919, 3.s., **43,** 1116-1120; Abst. Presse Méd. (Paris), **27,** 796.

The aim of this study was to obtain a method for the determination of the functional state of the endocrine glands in those cases in which the symptomatology is evasive or complex, by comparing the results of the effects of the administration of endocrine products in normal individuals and in those in whom obvious endocrine disturbance existed. The effect of the injection of extracts of the same gland may be quite different, however, depending upon the previous state of the functions of the endocrine gland stimulated to activity by the injection. In other words, the reacting tissue may have become sensitized. In acromegaly injections of hypophyseal extracts, even in large doses, is without effect. In subjects with typical exophthalmic goitre subcutaneous injections of hypophyseal extracts (posterior lobe) caused a notable but transitory slowing of the pulse and marked lowering of systolic pressure. In normal individuals, on the other hand, or in cases of tachycardia independent of thyroid conditions, the decrease of systolic pressure is slight and slowing of pulse does not occur. In thyroid insufficiency hypophyseal extracts gave rise to acceleration of the pulse, while systolic pressure was decreased as in normal subjects. The authors produced in 4 individuals presenting hypothyroid syndromes the reactions of hyperthyroidism by feeding desiccated thyroid in doses of .010 to .020 grams daily. Previous to the hyperthyroidization the patients responded to hypophyseal extract injections by accelerated pulse and the usual systolic pressure effects. After the administration of the thyroid preparations the same treatment with pituitary extract caused a lowering of the pulse rate. These facts are interpreted as indicating that a slowing of the pulse in a case of tachycardia after the injection of pituitary extract is evidence of a hyperactive thyroid. Adrenalin injections in the same subjects gave markedly abnormal increases in pulse rate. These reactions then are actually involved with increased thyroid activity; they have been repeatedly tested. It seems, then, that the presence in the organism of thyroid products in excess, either produced by the homologous gland or artificially introduced, favors the reactions to substances contained in hypophyseal extracts and adrenalin,

and induce phenomena sufficiently constant as to serve as a diagnostic measure for hyperthyroidism.—F. S. H.

(ENDOCRINE ORGANS) What fears and states of anxiety in a patient mean to the gynecologist. Bandler (S. W.), N. Y. Med. J. (N. Y.), 1920, **111**, 619-622.

Mental states and psychoses have a neurophysical basis and are not produced solely through psychic effects, but also by definite and specific endocrine activity. The adrenals and thyroid glands are the end-organs most closely related to fears, anxieties, and phobias. However, the corpus luteum is the primary factor which is responsible for these conditions, for the reason that a retained corpus luteum inhibits ovulation and excites disturbances in the thyroid and adrenal glands. Such a condition is combatable by the administration of ovarian extracts and suprarenal extract which contains the cortical material.—H. W.

(ENDOCRINE ORGANS) The instincts, the emotions and the endocrines in sterility. Bandler (S. W.), Med. Rec. (N. Y.), 1920, **97**, 383-391.

A lengthy article, containing much brilliant theorizing which is positively stated as proven, but most of it on very slender scientific basis. It is claimed that a large percentage of cases of sterility in women are not mechanical in origin and are unimproved by surgery, but can be cured by pluriglandular organotherapy. The author expects to publish a series of cases in which endocrine therapy was the only treatment given. [It is to be hoped that the cases will be reported in detail and the exact formulæ and dosage administered carefully recorded].—H. L.

(ENDOCRINE ORGANS) The balance between the endocrines and in each individual endocrine. Bandler (Samuel Wyllis), Med. Rec. (N. Y.), 1920, **97**, 638-647.

An elaborate consideration of the interrelationship of the ductless glands and their relation to the intellect, emotions, character, dreams, sleep, etc. The author goes so far as to believe that kidney diseases are due to endocrine abnormality, that fibroids and myomata of the uterus are the result of pituitary unbalance, that all tumors, benign and malignant, are due to endocrine action. "Many of the statements above made cannot as yet be substantiated by laboratory investigation; they have, however, stood the more convincing test of thera-

peutic application." [Those interested in such advanced and even startling ideas are referred to the original article, which does not readily lend itself to concise abstracting.]—H. L.

(ENDOCRINE ORGANS) The correlation of function; with special reference to the organs of internal secretion and the reproductive system. Bell (W. Blair), Brit. M. J. (London), 1920, **(i)**, 787-791.

The paper is a reproduction of a lecture delivered before the British Medical Association. The author is of the opinion that over-specialization on the part of the medical profession has led to the neglect of what he calls the "Correlation of Function" through the organs of internal secretion. Accordingly he advises the specialist, especially the gynecologist, to look beyond the confines of his particular anatomical territory for an explanation of the pathological conditions encountered.

The production of masculinity in woman by hyperplasia or neoplasia of the suprarenal cortex or anterior lobe of the pituitary is mentioned, as well as the fact that the pituitary body becomes permanently enlarged and changed in histological appearance in a woman after child-birth. This latter fact might be of use in medico-legal cases. The ovary is regarded as a means of maintaining the metabolism of the female at a higher level during the reproductive period, in order that she may nourish the child in utero and during lactation. Menstruation is regarded as "the monthly excretion of substances that would be concerned in the building up of a child were the woman pregnant." After the menopause the whole ductless gland system is involved. Atrophy of the thyroid coincident with atrophy of the ovaries has been demonstrated, and therefore thyroid extract is advocated in the treatment of mental conditions accompanying the menopause. Evidence is advanced to show that pituitary insufficiency is the cause of dystrophia adiposogenitalis. This is often produced by the pressure of a tumor on the stalk. Besides radiography, increased carbohydrate tolerance, subnormal temperature and low blood pressure may aid in diagnosis. The relation of the thyroid to the reproductive organs is also discussed.—L. G. K.

(ENDOCRINE ORGANS) Action of electrical currents on ductless glands and other tissues. De Kraft (F.), Med. Rec. (N. Y.), 1920, **97**, 136-138.

The author refers to the beneficial action of various forms of electricity in hyperthyroidism, obesity, amenorrhea, etc.

He believes that high frequency currents promote nutrition, check toxins, increase perspiration and elimination through the kidneys, restore luster, softness and moisture to the hair, improve the condition of the nails, increase metabolism, remove visceral congestion, etc. He mentions the uses of the diathermic, static wave and galvano-faradic-sinusoidal currents.—H. L.

(ENDOCRINE ORGANS) Results and active principles in organotherapy of abnormal menstruation (Über die Erfolge und das wirksame Prinzip der Organestrakttherapie bei Menstruationsstörungen). Esch (P.), Zentralbl. f. Gyn. (Leipzig), 1920, **44**, 561-568.

The influence of intramuscular organotherapy in abnormal menstruation is, according to the author, not due to a specific active principle, but may be observed after the injection of several kinds of proteins. Only the injection of hypophysis preparations may have a specific influence, as it causes contractions of the uterus.—J. K.

(ENDOCRINE ORGANS) Endocrinologist and internist. Herrick (W. W.), N. Y. M. J., 1920, **111**, 286-287.

The author sounds a note of conservatism relative to the present tendency to explain all things from an endocrine standpoint. Back of the endocrine organs and responsible for their disturbance lie other conditions, i. e., infections, metabolic disorders and psychic states.—H. W.

(ENDOCRINE ORGANS) Dietetic deficiency and endocrine activity, with special reference to deficiency œdemas. McCarrison (Robt.), Brit. M. J. (London), 1920, **(ii)**, 236-239.

Pigeons, guinea-pigs and monkeys were fed on diets deficient in the various vitamines. It was found that all endocrine organs, with the exception of the adrenals and the pituitary, undergo greater or lesser degrees of atrophy and depreciation in functional capacity in consequence of dietetic deficiencies. The adrenal glands and, in the male, the pituitary body, enlarge in consequence of dietetic defects, the former greatly, the latter slightly. The adrenals are the most susceptible of the endocrine structures to dietetic defects. The adrenin content of the enlarged adrenals varies with the character of the dietetic defect; it is in excess of normal when the food is deficient in vitamines, in proteins and disproportionally rich in starch; it is below normal when the diet is scorbutic, and also when concurrent infections are associated with diet-

etic defects. Oedema is invariably associated with massive enlargement of the adrenal glands in pigeons fed on autoclaved rice. But massive enlargement of the adrenals is not always associated with œdema. This association bears some intimate relationship to the adrenalin content of the enlarged organs, since when the content is high œdema occurs in 86 per cent of the cases and when the content is low œdema does not occur. Fresh butter contains some substance which tends to protect against œdema. This substance was not found in cocoanut oil. The hypothetical "anti-œdema" substance in butter has a pronounced influence over the adrenal glands. It appears to exert its protective action against œdema by maintaining their adrenalin content at a low level. Butter varies in its capacity to protect against œdema. This variation is dependent on the quality of the cow's food. Butter is richer in anti-œdema substance when the cows are fed on dry fodder. It is suggested that œdema is caused by the excess of adrenalin acting directly on the kidney to inhibit the flow of urine and to cause a retention of NaCl.—L. G. K.

(ENDOCRINE ORGANS) Grafts of glandular organs (Greffes d'organes glandulaires). Mauclaire (M.), Progrès Méd. (Paris), 1920, **35**, 345-349.

Mauclaire reviews the literature on organ grafting. Aside from the fact that citations of publication are lacking, the article is a valuable summary of available data. The topics treated are: thyroid grafts in animals and men; parathyroid grafts; thymus grafts; ovarian grafts in animals and in women; testicular grafts in animals and men; renal grafts in animals and men; adrenal grafts in animals and men, and, finally, in less detail, grafts of spleen, pancreas, salivary and mammary glands, hypophysis, prostate and liver. In each case the methods used, animals upon which the experiments were made and, to some extent, results are treated. The article, being itself a summary, can not be abstracted. It is concluded that although this type of work offers many difficulties, and more experience is necessary, the results already secured are very encouraging.—R. G. H.

(ENDOCRINE ORGANS AUTONOMIC N. S.) The patient's reaction: a neglected but important phase in the study of medicine. Pottenger (F. M.), Annals of Medicine (Haggerston, Md.), 1920, **1**, 52-54.

Pottenger points out the intimate relationship between the psychic factors and the symptomatology of disease and empha-

sizes the part played by the endocrine and autonomic systems in the evolution of disease pictures. The burden of the article is that these factors should receive relatively much greater attention at the hands of practical clinicians. [That they do not receive adequate attention is probably due to the paucity of definite diagnostic criteria in the fields of endocrinology and visceral neurology. It is the obvious duty of workers in these fields to establish such criteria.]—R. G. H.

(ENDOCRINE ORGANS) The skin as an index to health. Scholtz (M.), Med. Rec. (N. Y.), 1920, **97**, 824-828.

Scholtz calls attention to the relation between skin disorders and systemic diseases and mentions the syphilis syndrome, tuberculosis syndrome, diabetic syndrome, erythema multiforme group and focal infection, the leukemic syndrome, the precancerous syndrome and the endocrinous syndromes. A thick, dry, pasty skin, suppression of perspiration, lusterless brittle hair and alopecia suggest hypothyroidism; and many cases of chronic eczema, psoriasis, ichthyosis and scleroderma are improved by administration of thyroid. Hyperthyroidism produces thin, perspiring, easily flushed skin, urticarial attacks, pigmentation, dystrophies of the nails, keratinization and pruritis. The author mentions the bronze-like skin of Addison's disease and the successful treatment of some cases of vitiligo by extract of suprarenal. Fibromatous growths, warts, alopecia in men and hypertrichosis in women are sometimes due to hypophyseal disease. He also refers to the skin changes accompanying pregnancy and following castration, and to the angioneurotic dermatoses of Raynaud's disease, scleroderma, angioneurotic edema, etc.—H. L.

(ENDOCRINE ORGANS) Changes in the endocrine organs, especially the adrenal cortex, following occlusion of the pancreatic duct (Ueber die Veränderungen der endokriner Organe, besonders der Nebennieren-Rinde nach der Unterbindung des Ductus pancreaticus und ihre Bedeutung). Tokumitsu (Yoshitomi), Venhandl. d. japan. path. Gesellsch. (Tokyo), 1916, **6**, 21-23.

The first effect of tying the pancreatic duct in rabbits is a general atrophy of the pancreas. Subsequently the islands of Langerhans regenerate to, or above, the normal mass. In the adrenals the cortex becomes hypertrophic; the medullary cells become smaller and more thickly crowded and give a clearer chromophil reaction. The thyroid enlarges. In the hypophysis the eosinophil cells decrease and the "Hauptzellen"

increase. For a short time after the operation glycosuria can be produced with a smaller quantity of adrenin than in case of normal animals. Destruction of the adrenal cortex by knife or cautery causes, in itself, no glycosuria, but after tying the pancreatic duct such measures in the adrenals produce definite glycosuria. Normal rabbits die from the loss of ¾ of the adrenal cortex, but after occlusion of the pancreatic duct the loss of ¼ of the cortex is fatal. When thyroidectomy is combined with the above procedures glycosuria is prevented. On these data the author postulates a functional antagonism between the thyroid and the pancreas.—R. G. H.

ENDOCRINOPATHIES (Syphilis hereditaire tardive; endocrinopathies; hypophyse. Castex (M. R.) & Waldorp (C. P.), La Prensa Med. Argentina (Buenos Aires), 1920, **6,** 309.

A report of certain clinical observations and a critical study of the topic. The authors believe that hereditary syphilis is a factor in acromegaly and that the same factor is involved in most cases of gigantism. Similarly it may produce infantilism and the Fröhlich syndrome.—B. A. H.

(ENDOCRINOPATHIES) Hereditary syphilitic terrain and its relation to tuberculosis (El terrena heredo espicifics y sus relaciones con la tuberculosis. Mariño (E.) & Barilari (M. J.), Prensa med. argent. (Buenos Aires), 1920, **6,** 312.

Hereditary syphilis produces lymphatism, asthenic habitus and numerous endocrin dysfunctional states. Tuberculosis is often implanted in this soil. Amelioration is to be expected, in such cases, rather from tuberculin than mercury. —B. A. H.

Medical aspects of ENDOCRINOLOGY. Hertz (J. J.), Med. Rec. (N. Y.), 1920, **97,** 511-514.

A brief, fragmentary resume of some disturbances of the thyroid, parathyroids, adrenals, pituitary and pancreas with some suggestions regarding appropriate organotherapy; no new data.—H. L.

The position of ENDOCRINOLOGY in general medicine (Posicion dela endocrinologia en la medicina general). Marañón (G.), Real Acad. Nat. de Med. (Madrid), 1918, —, —.

Interesting general review of the glands of internal secretion in many diseases and syndromes the pathogeny of which is little known.—E. B.

GASTRIN Studies. V. Chemical studies on gastrin bodies. Koch (F. C.), Luckhardt (A. B.) & Keeton (R. W.), Am. J. Physiol. (Balt.), 1920, **52,** 508-520.

This is the fifth of a series of studies of gastrin bodies, the other papers of which have appeared in the Am. J. of Physiol., Vols. **37, 50** and **51.** This paper is a report of observations bearing more particularly on the chemical phase of the work. Various chemical procedures are described and the results noted. The conclusions drawn are as follows:

(1) A striking similarity exists between the effects of histamin and gastrin. (2) Gastrin appears to be more stable than secretin is reported to be, although they are similar in many respects. (3) Gastrin has not been precipitated by picric or picrolonic acid. (4) Gastrin appears to be a basic imidazol derivative which can be extracted as the free base by amyl alcohol. (5) Thus far histamin and pilocarpin are the only known imidazol derivatives which stimulate the gastric mechanism to secretion. (6) Choline acts with uncertainty and then only faintly as compared with histamin or gastrin.

—T. C. B.

(THYROID) Goiter. Cooke (A. B.), Calif. State. J. M. (San Francisco), 1920, **18,** 82-83.

No new data.—H. W.

(THYROID) Goiter. O'Day (J. C.), N. Y. Med. J. (N. Y.), 1920, **111,** 503-505.

Goiter may be defined as a partial or complete enlargement of the thyroid gland. Any benefits derived from the ligation of the thyroid arteries is due merely to the rest subsequently imposed. Focal infections cannot be considered as causative factors in the production of goiter, for the Hawaiians, although extremely subject to focal infections, do not develop goiter.—H. W.

Modern treatment of STERILITY. Armitage (H. M.), N. Y. Med. J. (N. Y.), 1920, **111,** 360-363.

Defective implantation of the ovum is indicated in women who frequently miss a menstrual period and go over 10 to 14 days and then flood. Such cases should be treated with corpus luteum extracts inasmuch as the corpus luteum of the individual is not sufficient to bring about complete implantation of the ovum. Profuse menstruation is due to over-stimulation

of the endocrine organs and should be treated with preparations of thymus gland and mammary substance. Irregular menstruation often yields to the administration of thyroid, ovary and corpus luteum substances.—H. W.

(GONADS) A case of human bilateral hermaphroditism with bisexual glands (Un cas humain d'hermaphrodisme bilateral a glandes bisexuelles). Briau (E.), Lacassagne (A.) & Lagoutte (M.), Gynec. et Obst. (Paris), 1920, **1**, 155-179.

An extensive and detailed report of a case of bilateral hermaphrodism including the macroscopic and microscopic appearance of the abnormal genitalia. The individual possessed the efferent passages normal to both sexes, a uterus the dimensions of which would be admitted as those of a nullipara, two tubes of normal sizes and structure and spermatic cords each segment of which was normal. Moreover, there occurred bilaterally a mixed sex gland containing both ovarian and testicular tissue. The left gland was within the pelvis and presented the aspects of a functioning ovary together with spermatogonia producing testicular tissue, an ovotestis of predominantly ovarian function. The right gland was within the inguinal canal, possessed an epididymus and vas deferens, had produced spermatocytes and contained ovarian fragments. This the authors consider as an ovotestis predominantly testicular in function.—F. S. H.

Gonads, Histogenesis of the —— (Sobre la histogènesi de la glandula genital). Domingo (P.) & Vilaseca (S.), Treballs de la Societat de Biologia, Barcelona, 1918, **6**, 51-61, 11 pl.

The article is largely of technical histological interest. As regards the interstitial cells of Leydig, the authors remark that their origin has been much debated. They, themselves, believe the cells to be derived by successive differentiations from certain mesenchymatous cells in relation to the tunica albuginea and of the interlobular tissue and the walls of the tubules. In the testes of the human fetus the authors have recognized also certain interstitial cells which are voluminous, with clear protoplasm and irregular contour and transparent, spherical nuclei. Among them many mitoses are seen and multinucleate cells are observed. They seem to be analogous with the primordial ovules. The article is illustrated with eleven photomicrographs.—R. G. H.

(GONADS) The question of hermaphrodism in man and mammals (La question de l'hermaphrodisme chez l'homme et les

mammifères). Lacassagne (A.), Gyn. et Obst. (Paris), 1920, **1**, 273-296.

A bibliographic review.—F. S. H.

(GONADS) A case of pseudohermaphroditismus masculinus internus with tumor of testicle (Over een geval van pseudohermaphroditismus masculinus internus met gezwelvorming van den testikel). Lauwers (G. B.), Inaug. Dissertation (Amsterdam), 1920.

The patient, who had normal sexual desires, was operated upon for hernia. Death by embolus followed. Post-mortem examination showed: Penis, bladder and rectum normal. On both sides the vasa deferentia were normal. Behind the bladder a mass of tissue was noted in which two Fallopian tubes were found and a uterus bicornuus. The right testicle contained a carcinoma. A very good bibliography on tumors of testicles and hermaphroditism is included.—J. K.

(GONADS) The production of artificial hermaphrodites in mammals. Moore (Carl R.), Science (N. Y.), n. s. **52**, 179-182.

A criticism of the works of Steinach and Sand (Endocrin., **4**, 266). "Steinach was unable to obtain either a growth or persistence of an implanted sex gland unless the gland of the host (gland of the opposite sex) was removed before the implantation was made."

Sand supports Steinach on the whole. "In explaining his failure to obtain growths of ovarian grafts in non-castrated infantile male animals he assumes a rather indefinite type of 'Immunity' on the part of the host towards the implanted tissue." Moore has been able to obtain growths of ovarian grafts, subcutaneously, intramuscularly and intraperitoneally in young male rats which had one sex gland intact and normal. The graft, eight and one-half months after implantation, presented all of the features of a normal ovary of similar age excepting corpus luteum tissue and the presence of a large number of atretic follicles. The behavior of the follicles of the grafts is similar to the corresponding structures of the young female sex gland before the age of sexual maturity. Mammalian testicular transplantation results in the loss of the germinal epithelium. "The grafts resemble a cryptorchid testis in that both retain the well-rounded seminiferous tubules, but all that remains of a cellular character are Sertoli cells. The testis graft does persist after transplantation in a female, with an

intact ovary, and it is as normal as autoplastic testicular grafts. either with or without previous castration. A male rat with one testis will function as a normal male during the time it is carrying two ovarian grafts as an integral part of its somatic structure."—F. A. H.

GYNECOMASTIA and the theory of a mammary internal secretion (Zur Kenntniss der Gynäkomastie und zur innersekretonischen Theorie der Brustdrüse). Novak (J.), Zentralbl. f. Gynäk. (Kiel), 1919, **43**, 253-258.

A report of 5 cases of gynecomastia and a discussion of the existing theories of mammary secretion. No new data. —F. S. H.

Experimental HERMAPHRODITISM, historical remarks on—(Historische Beitrag zum experimentellen Hermaphroditismus). Foges (A.), Wien. klin. Wchnschr., 1920, **33**, 224.

Data reported elsewhere. See Endocrin., **4**, 265. —J. K.

(HORMONES) Hormonal stimulation of the brain (Delas estimulaciones hormonales del encefalo). Mouchet (E.), Prensa med. argent. (Buenos Aires), 1920, **6**, 306.

Since the brain receives not only nerve stimulation but also blood, the author deduces that the mental state is dependent upon hormone as well as nervous influences.—B. A. H.

HYPERTHYROIDISM. Webster (A. B.), N. Y. Med. J. (N. Y.), 1920, **111**, 283-284.

After discussing the relation of focal infections to thyroid disturbances, the author bewails the fact that "surgery has gone mad in treating end results and not dealing with the primary cause," and then proceeds to justify surgical procedures on the abnormally functioning thyroid gland. However, he fails to state whether toxines or the thyroid itself is primarily at fault, or whether the condition in the thyroid is or is not the end result of altered functions in other parts of the body. —H. W.

(HYPOPHYSIS) The pathogenesis of diabetes insipidus. Bauer (J.) & Aschner (B.), Wiener. Arch. f. inn. Med., 1920, **1**, 297-334.

The authors give in tabular form an extensive series of metabolic findings in a typical case of diabetes insipidus in a

woman who had been under observation for ten years. They believe that diabetes insipidus may find its origin in the kidney or its innervation. This is often observed in the familiar constitutional form of the disease. A disease in the neighborhood of the nerve centres of the midbrain or fourth ventricle is the most ordinary cause. Nearly all cases in literature belong to this type. A primary change of the center for thirst perception in the cortex of the brain may combine itself with an irritation of the subcortical diuresis center. In this way psychical influences may act. It has never been definitely proved that the hypophysis itself may be the cause of diabetes insipidus. Even with loss of the diuresis regulating property of the hypophyseal secretion normal compensatory processes in the kidneys themselves may suffice to prevent diabetes insipidus.—J. K.

(HYPOPHYSIS) Radium therapy of tumors of the hypophysis, with syndrome of acromegaly (Radiumterapia nei tumori ipofisari a sindrome acromegalica). Bertolotti (M.), Radiol. med. (Milano), 1919, **6**, 315.

A number of cases have now been treated by radiation with some favorable results, and a notable improvement in several. As there is great variation in the symptoms according to the position of the tumor, this may account for variation in the results of treatment, and the negative results of X-ray therapy in some cases. In dystrophy from tumor of the hypophysis the author's own results have been unfavorable; similarly the clinical results of all tumors are varied, and the course of the disease may be from 2 to 59 years. In benign cases X-rays are advisable and useful. The detractors of X-rays assert that the improvement is a natural retrogression, but this is always of short duration, whereas the improvement after X-rays lasts much longer. The best results are obtained in early cases, and, as cystic degeneration follows in acromegaly, X-rays should be applied before this sets in. The author gives the history of a case treated by the gamma-rays of radium from the early days.

The first symptoms were seen in May, 1917, and by December the condition was already far advanced—vision nearly gone, impotency, asthenia, etc.—so that an adenoma or adenocarcinoma of the pituitary was suspected, most probably of the anterior lobe and of rapid and malignant development. A course of intensive radium treatment was begun, but by March, after two treatments, the patient was worse instead of better and the condition seemed desperate. Not till July was there

a slight improvement, when the vision of the left eye began to increase. Continuous though slow progress was made, and in September the radiograph showed surprising improvement in the profile of the sella turcica.

By December, 1918, the vision had so far recovered that the patient was able to resume his work as a designer, and all the symptoms had disappeared. This result was obtained solely by massive doses of radium applied bi-temporally, and neither the intrabuccal nor the intranasal method was employed. It follows that the rays are efficient at a distance of more than 10 cm. through tissues, and have probably an elective action on certain neoplastic cellular elements.—Med. Sc. Abst. & Rev., **2**, 204.

(HYPOPHYSIS) Permanent experimental polyuria (Polyurie expérimental permanente). Camus (J.) & Roussy (G.), Compt. rend. Soc. de biol. (Paris), 1920, **83**, 764-765.

A description of two cases of permanent experimental polyuria in dogs. Of endocrine interest is the statement that it is not the ablation of the hypophysis which determines the polyuria, but the superficial lesion of the base of the brain corresponding to the opto-peduncular space.—T. C. B.

(HYPOPHYSIS) A case of acromegaly (Sobre un caso de a.). del Cañizo (A.), Siglo Méd. (Madrid), 1917, ——, ——, (Nov. 17.)

A case is presented which manifested all the typical symptoms of acromegaly, but with certain other features worthy of comment. The condition developed at the unusually late age of 53 years. Especially interesting is the fact that the thymus was enlarged, as was demonstrated both by percussion and radioscopy; it was so pronounced as to give rise to frank symptoms of mediastinal pressure. The author discusses the possible relationship of the hypophysis and thymus to the development of the osseous tissues (citing the alleged production of experimental rickets through thymectomy by Klose, Vogt and Matti) and of the genital apparatus. Thymic hypertrophy in eunuchs is not unusual and in such a process as acromegaly, in which sexual activity is diminished, a similar enlargement of the thymus, as in this case, might be expected.—E. B.

(HYPOPHYSIS) A case of syphilitic diabetes insipidus (Ein Fall von Diabetes insipidus auf luetischer Basis). Chiari, Wiener klin. Wchnschr., 1920, **33**, 620.

A woman of 30 manifested cessation of menstruation, polyuria and polydipsia and multiple swellings of the bones. The quantity of urine reached 15 liters daily, with a specific gravity of 1001. The Wassermann reaction was positive. She was cured by antiluetic treatment. The author believes that a syphilitic change in the hypophysis or in the regio subthalamica was responsible for these symptoms. A skiagram showed no pathological changes.—J. K.

(HYPOPHYSIS) Study of a case of diabetes insipidus with special reference to the mechanism of diuresis and the action of pituitary extract upon it. Christie (C. D.) & Stewart (G. N.), Arch. Int. Med. (Chicago), 1917, **20,** 10-23.

A careful series of studies was made upon a female subject who excreted up to 20 liters of urine daily. She reacted well to pituitary extract but required doses of 2 cc. repeated three times in each 24 hours to maintain the effect. The relative hydration of the blood was investigated by determinations of electrical conductivity and by hematocrit readings of the blood. The relative volume of the serum was found to be slightly diminished and the conductivity slightly decreased, showing that the extract caused a slight dehydration of the blood. By Stewart's calorimetric method it was determined that the blood flow through the hands was increased during the period of reaction to the pituitary extract, hence the renal flow was probably decreased. Functional tests indicated that the diuresis was not in any way associated with pathological alterations in the kidneys.—R. G. H.

(HYPOPHYSIS, ADRENAL, THYROID) Hemostatic medication (Médication hémostatique). Dalché (P.), La Gyn. (Paris), 1920, **19,** 139-152.

A discussion of the various causes and treatments of genital hemorrhages in the female. Consideration is given to the use of the directly acting vaso-constrictor properties of hypophyseal and adrenal extracts and to the indirect activity of thyroid opotherapy in such conditions as the metrorrhagias of myxodema and obesity. Note is also made of the favorable coagulative action of the posterior lobe of the hypophysis.
—F. S. H.

HYPOPHYSIS opotherapy with favorable action in a case of obesity and diabetes insipidus (Action favorable de l'opothérapie hypophysaire dans un cas d'obésité et de diabète

insipide). Flandin (Ch.), Huber (J.) & Debray (M.), Bull. et. mem. Soc. med. d. hôp. (Paris), 1920, 3. s., **44,** 487-490.

A new example of the action of hypophyseal extracts on the polyuria of diabetes insipidus. In this case the urinary output of the woman, which was around 14 liters per 24 hours, was lowered to values of 10, 12 and even 6 liters as the result of the administration of the drug, although the effect was in general but transitory. No effect was observed as regards diminution of the obesity.—F. S. H.

(HYPOPHYSIS) Dystrophia adiposo-genitalis. Foerster, München. med. Wchnschr., 1920, **67,** 675.

Description of a case. The patient suffered from this disease for 20 years. There were headaches and some slight signs of acromegaly. The skiagram showed the sella turcica to be enlarged. The author diagnosed a benign tumor of the hypophysis.—J. K.

(HYPOPHYSIS) Dystrophia adiposo-genitalis. Hannema (L. S.), Nederl. Tijdschr. v. Geneesk. (Haarlem), 1920, **64,** 2434-2435.

The case is recorded of a boy of 13 years with polyuria, adiposity and extremely small genitals. There were no neurological nor any eye symptoms. Sugar tolerance was much increased. No enlarged sella turcica was detectable radioscopically.—J. K.

HYPOPHYSIS, A doubtful case of tumor of — (Een twijfelachtig geval van hypophysis gezwel). Hannema (L. S.), Nederl. Tijdschr. v. Geneesk. (Haarlem), 1920, **64, (I),** 2436-2438.

A woman of 34 for 4 years suffered much with headache. There was no vomiting, no eye symptoms and no polyuria. Recently her face has become broader and her feet have become larger and hairs have developed on breast and legs. Sugar tolerance is diminished. Radioscopically the sella turcica appears very large but of a perfectly normal form. There are certain hysterical symptoms and it is certain that the patient exaggerates her complaints. A tumor of the hypophysis is probable but not at all certain since a large sella with normal shape may be seen in healthy individuals.—J. K.

(HYPOPHYSIS) On the relation between the interstitial cells and the hypertrophy of the hypophysis. Hayami (T.), Verhandl. d. jap. path Gesellsch. Tokyo, 1919, pp. 43-44.

In order to determine which constituent of the testis is responsible for the hypertrophy of the hypophysis which usually follows castration, the author experimented with rabbits about three months old, which he divided into groups and treated as follows: (1) Double castration; (2) Castration on one side and vasectomy on the other; (3) Double vasectomy and treatment of the testicles with Röntgen rays. He studied only animals which lived for four months or more after the operation. Double castration produced the usual hypophyseal hypertrophy. Castration and vasectomy caused hypophyseal hypertrophy together with an almost complete cessation of spermatogenesis and an increase in the number of the interstitial cells in the remaining testes. Double vasectomy and treatment with Röntgen rays destroyed the epithelial and Sertoli cells and increased the interstitial cells, which must, therefore, in his opinion, be responsible for the resultant enlargement of the hypophysis.—E. V. C.

(HYPOPHYSIS) Occurrence of polyuria (diabetes insipidus?) in a case of epidemic encephalitis [Auftreten von Polyurie (Diabetes insipidus?) im Verlaufe eines Falles von Encephalitis epidemica]. Hoke (E.), Wiener klin. Wchnschr., 1920, **33**, 562.

During an attack of encephalitis lethargica polyuria (up to 10 liters daily) developed. When pituglandol was injected the quantity of urine was diminished to about 3 liters. The patient is still under treatment.—J. K.

HYPOPHYSIS extracts, Action of—on diuresis in the dog and rabbit (Accion de los extractos de hipófisis sobre la diuresis en el perro y el conejo). Houssay (B. A.), Galan (J. C.) & Negrete (J.), Soc. de Biol. de Buenos Aires, June 10, 1920.

The action of hypophyseal extracts upon diuresis is essentially different in case of different animals. In the rabbit one sees oliguria and anorexia, while in the dog there results an augmentation of diuresis except following profuse ingestion of water. It can not be determined, therefore, from the effects of such extracts in case of any one species of animal whether or not the hypophysis exercises a physiological influence upon diuresis—B. A. H.

HYPOPHYSIS Study of the carbohydrate tolerance in Eck fistula and hypophysectomized animals (posterior lobe removal). Liver function in the metabolism of sugars. Jacobson (Conrad), Am. J. Physiol. (Balt.), 1920, **52**, 233-247.

In animals deprived of the hypophysis there is a rise in sugar tolerance, and this rise can be lowered by administration of the extract of the posterior lobe. The lowering of the sugar tolerance is evidenced by hyperglycemia as well as glycosuria, and efforts have been made to determine the source of this glycogen. Good sized healthy dogs were used. A typical lateral anastomosis between the portal vein and inferior vena cava was made. The portal vein was ligatured in two places and cut between the ligatures, close to the liver hilus. The posterior lobe of the pituitary was removed by the intracranial method of Crowe, Cushing and Homans. The paper is largely concerned with sugar tolerance in Eck fistula animals, but the conclusion is reached that the glycogenic capacity of muscle is increased following posterior lobe removal in an Eck fistula animal as in an intact animal. The augmentation is, however, considerably slower. No augmentation of levulose tolerance is noted—T. C. B.

HYPOPHYSIS, Modern physiology and pathology of— (Der jetzige Stand der Physiologie und Pathologie der Hypophyse). Jacoby (M.), Deutsche med. Wchnschr. (Berlin), 1920, **46**, 742-743.

A general review without new facts. The author points out once more that it is necessary in diseases of one endocrine organ to consider the others as all these organs have a mutual influence on each other.—J. K.

Ossification of HYPOPHYSIS causing diabetes insipidus (Uber einen Fall von Verknocherung der Hypophysis, die Diabetes insipidus verursachte). Kawakita (S.), Verhandl. d. jap. path. Gesellsch., 1919, ——, 45-54.

Relates the case of a woman of 30 years in which diabetes insipidus was definitely associated with retarded development of the internal genitalia.—E. V. C.

(HYPOPHYSIS) Observations on two cases of diabetes insipidus, with account of the literature relating to association between pituitary gland and this disease. Kenneway (E. L.) & Mottram (J. C.), Quart. J. Med. (Lond.), 1919, **12**, 225-228.

The authors studied the composition and molecular concentration of the urine in comparison with that of the blood

serum in two cases of diabetes insipidus. When large amounts of sodium chlorid are given the urine output is so adjusted that the percentage of nitrogen plus that of the chlorin in the urine remains constant. The kidney, therefore, has not the power of concentration normally demonstrable after the ingestion of salt. The antidiuretic effect of pituitrin was demonstrated both in a normal subject and in a case of diabetes insipidus. It was found that hypodermatic administration but not administration by mouth, was effective. The writers could find no instance in the literature of diabetes insipidus in which hypophyseal abnormality was excluded definitely by autopsy observations, whereas, in a number of cases the posterior lobe of the hypophysis was definitely involved. Lesions of this structure are, however, not always accompanied by diabetes insipidus. The morphologic evidence is therefore not conclusive. Therapeutic evidence, however, is convincing that the hypophysis normally plays a part in the regulation of renal activity.—R. H. G.

(HYPOPHYSIS) Two cases of adiposo-genital syndrome of hypophyseal origin in the adult (Sur deux cas de syndrome adiposo-génital d'origine hypophysaire chez l'adulte). Lereboullet (P.) & Hutinel (J.), Bull. et mem. Soc. med. d. hôp. (Paris), 1919, 3. s., **43**, 745-754.

Case reports. No new data.—F. S. H.

HYPOPHYSIS, State of the—in encephalitis lethargica (État de l'hypophyse dans l'encéphalite léthargique). Marie (P.) & Tretiakoff, (C.), Bull. et mem. Soc. med. d. hôp. (Paris), 1920, 3. s., **44**, 357-358.

Presentation of histological preparations of specimens of the hypophysis from two cases of encephalitis lethargica. The subjects were markedly somnolent during the progress of the disease. Macroscopically the glands were slightly congested without being notably swollen. On sectioning, a moderate diffuse congestion unaccompanied by leucocytic infiltration was evident. No appreciable alterations of the cells of either lobe could be seen. No gross lesions of the hypophysis were observed in these two cases, but in one case a small hemorrhagic area 2 to 3 mm. in diameter, accompanied by necrosis of glandular cells without leucocytic reaction, was found, while in the other case there appeared to be quite a number of blackish pigment granules disseminated among the cells or included in the protaplasm. Nevertheless, the au-

thors conclude that symptomatology of lethargic encephalitis cannot be explained by the condition of the hypophysis.
—F. S. H.

(HYPOPHYSIS) Diabetes insipidus in a baby. Narigawa (S.), Jikwa Zasshi (Japan), 1918, No. 213, 16-26.

There was no disturbance of renal function nor of blood pressure. Under treatment, which consisted of injections of 0.29 mil. of pituitary extract, there was improvement. The volume of urine decreased and the concentration of sodium chloride increased. (Abst. in China Med. J.)—L. G. K.

(HYPOPHYSIS) Two cases of hypophyseal adiposity with dwarfism (Zwei Fälle von hypophysärer Adipositas mit Zwergwuchs). Peritz (G.), Deutsche med. Wchnschr., (Berlin), 1920, **46**, 613.

Both cases are of syphilitic origin. The first subject is a girl of 14 with idiocy and a spastic paresis of the left side of the body. Her height is 123 cm. and weight 28.8 K. She shows typical adiposity. The second case is that of a boy of 3 years, with a weight of 12.8 K. and height of 82 cm. The skiagram shows an enlarged sella turcica. Intraspinal pressure is high. Probably there is here a hydrocephalus with resulting pressure on the hypophysis.—J. K.

(HYPOPSYSIS) Hypophyseal dwarfism (Hypophysärer Zwergwuchs). Priesel (A.), Deutsche med. Wchnschr., (Berlin), 1920, **46**, 704.

A short note on a case. The patient was 90 years old. There were pathological changes in the neurohypophysis and an abnormal sinus in the splenoid.

(HYPOPHYSIS) Acromegalia y diabetes insipida. Pittaluga (G.), Siglo Med. (Madrid), 1920, **67**, 90-93.

Description of a case of acromegaly with intense diabetes insipidus. The author favors the hypopituitary theory of etiology of the diabetes, explaining such cases of acromegaly accompanied by polyuria as produced by the mechanism indicated by Falta, Marañón and others, namely, compression of the median and posterior lobes of the hypophysis by the hypertrophic anterior lobe. The condition may spontaneously be relieved as the compression subsides or the parts become anatomically or functionally adapted to the compression.
—G. M.

(HYPOPHYSIS) Extensive destruction of the sella turcica without clinical symptoms. Rosenheck (C.), N. Y. Med. J. (N. Y.), 1920, **111**, 554-555.

Case report of extensive destruction of the sella turcica in a man of 60 years without clinical manifestations.
—H. W.

Sarcoma of the HYPOPHYSIS with acromegaly extirpated by the frontal route (Sarcoma de la hipófisis con sindrome acromegalico. Extirpacion por via frontal, etc.). Sacco (A.) & Del Valle (D.), Asoc. Méd. Argentina, Sec. Chirujia, July, 1920.

The authors describe a case of acromegaly with grave visual disorders in which extirpation of the hypophysis was performed. The ablation was regarded as complete. The Frazier operation, i. e., ablation with aspiration, was performed. Thereafter a considerable improvement of the vision was noted, and this progressed, but marked glycosuria and other diabetic symptoms supervened.—B. A. H.

(HYPOPHYSIS) A case of diabetes insipidus. Schnabel (Truman G.), & Gerhard (Arthur H.), N. Y. Med. J. (N. Y.), 1920, **111**, 812-815.

Report of a case of diabetes insipidus with symptomatic arrest following the hypodermic use of pituitrin. Over three years have elapsed since the onset of the disease and over two years since the cessation of symptoms. The hypodermic use of pituitrin was followed by a very immediate antidiuretic effect. Sterile water, corpus luteum and adrenalin used hypodermatically were without effect. Extract of pituitary gland by mouth was ineffectual. The specific gravity of the urine, while still fixed at a low figure (1.012), was raised to a relatively higher one. Contradictions from the literature are cited to illustrate the uncertain status of renal output in relation to pituitary function.—Authors' Abstract.

(HYPOPHYSIS) Note on the presence of iodine in large quantities of sheep pituitary gland. Seamen (E. C.), J. Biol. Chem. (Balt.), 1920, **43**, 1-2.

No iodine was found in three lots of 30, 50 and 100 grams of sheep pituitaries.—F. S. H.

HYPOPHYSIS, Contribution to the study of the— (Contribución al estudio de la hipofisis). Silva (A.), Innaug. Dissertation, Santiago de Chili, 1917.

It was concluded from a series of experiments that in the normal subject hypophyseal extracts give a transient or prolonged vascular hypotension. Such extracts give, however, a unique reaction in the active form of tachycardia of Graves' disease. This is sufficiently characteristic as to serve as a diagnostic criterion. In this disorder the extracts give not only hypotension but also polyuria, transient glycosuria, pallor of the skin and contractions of the intestines and uterus. (Relative threshold values are not stated.—Ed.) The extracts appear to give rise also to phosphaturia.—J. R. P.

(HYPOPHYSIS) X-ray treatment of visual disorders or hypophyseal origin (Le traitment par les rayons X des troubles visuels d'origine hypophysaire). Terrien (F.), Arch. d'opth. (Paris), 1916, **5**, 257-286.

Terrien analyzes eight cases from the literature and adds two others,—one of his own and one of Prof. Lapersonne's. The article includes a valuable detailed discussion of technique. The rays can be sent either through the temples or through the mouth, but the latter is usually preferable. A one millimeter aluminum screen is used and 5 H. units administered. Experience has shown that no fear need be entertained of injury to the brain. The results obtained have been mostly satisfactory. The headaches have in most cases ceased at once and the visual acuity and visual fields improved. The somatic hyperplasia of the acromegalics has not diminished, however. Radiations should be administered only during the period in which the hypophyseal function is in an augmented state, since their action is to diminish the activity of the gland. When the process has reached a destructive stage the radiation can only hasten the appearance of symptoms of hypophyseal insufficiency. X-ray therapy has the outstanding advantage that, being harmless, it can be utilized early in cases in which indications for surgical intervention are lacking.—R. G. H.

HYPOPHYSIS extract, The action of—on peristalsis (Der Einfluss des Hypophysenextraktes auf die Peristaltik). Zondek (B.), Arch. f. d. ges. Physiol. (Bonn), 1920, **180**, 68.

Zondek has studied the action of the glandular extract by direct observation of the intestine through a permanent window of celluloid healed into the abdominal wall; the method

is that of Katsch and Borchers. By each injection of the drug there is a preliminary "psychic shock" which lasts two minutes, with complete interruption of peristalsis. The hypophysis extract stimulates peristalsis of the large intestine, but occasionally first causes slight inhibition. It also regulates peristalsis. Injections of the drug are recommended in postoperative intestinal atony.—Med. Sc. Abst. & Rev., **2**, 494.

INTERNAL SECRETIONS, Influence of—on blood pressure and the formation of bile. Downs (A. W.), Am. J. Physiol. (Balt.), 1920, **52**, 498-507.

In a previous paper (See Endocrin., 1919, **3**, 214), the author describes the effect of various internal secretions on the formation of bile. In the present paper the relation between blood pressure and bile is considered. The gland substances employed were mammary, orchic, ovarian, pancreatic, splenic, thymic, and thyroid. Adrenalin and secretin were also investigated.

There seems to be no constant relation between blood pressure and the amount of bile secreted. Adrenalin causes a rise of pressure and increased bile formation, while secretin, if it has any influence, lowers blood pressure and increases bile production. There was no constant relationship between blood pressure and bile production after the administration of thyroid. The experiments indicate that some at least of the endocrine organs exert a specific influence on the secretory activity of the hepatic cells leading to the production of bile.

—T. C. B.

INTERNAL SECRETIONS, Influence of—on the tumors of the dog (Influence des la sécrétion interne sur les tumeurs des chiens). Korentchevsky (V.), Compt. rend. Soc. de biol. (Paris), 1920, **83**, 779-781.

The results of experiments on fifty-two dogs inoculated with sarcoma. In some the thyroid was removed, others were castrated; all were controlled. Castration and thyroidectomy clearly augmented the growth of sarcoma in the majority of cases. In all the animals, controls as well as operated, the tumors suffered retrogression and absorption as follows: Controls, 79 per cent; castrated, 56 per cent; thyroidectomized, 28.6 per cent. The introduction of a suspension of fresh testicle arrested the growth of the tumors, and accelerated their retogression.—T. C. B.

INTERNAL SECRETIONS, Influence of—on the tumors of mice (Influence des la sécrétion interne sur les tumeurs des souris). Korentchevsky (V.), Compt. rend. Soc. de biol. (Paris), 1920, **83,** 783-785.

The influence of castration on the growth of carcinoma in mice was not clearly manifested. Extirpation of the spleen and the genital glands resulted in an increase in strength and rapidity of the growth of chondromata. This did not seem to be true for the extirpation of the spleen only. In general the same was true for carcinoma, but the results are not so clear cut. Thyroid alimentation diminished the percentage of successful inoculations and retarded the growth of carcinomata, and this was most marked with small doses. In thymus feeding also, the greatest percentage of unsuccessful inoculations and the smallest tumors, where successful, were furnished by the group receiving the smallest doses of thymus. The small doses probably stimulated the defensive oncolytic forces, retarding growth or preventing the tumor cells from implanting themselves in the organism. Pituitrin had no effect. The author concludes from his studies that the state of the glands of internal secretion may be one of the important conditions determining the non-receptivity towards tumors.—T. C. B.

INTERNAL SECRETIONS, Influence of—and of autolysate on the tumors of rats (Influence des la sécrétion interne et des l'autolysat sur les tumeurs des rats). Korentchevsky (V.), Compt. rend. Soc. de biol. (Paris), 1920, **83,** 781-783.

Experiments were made on rats, the tumor being a fusiform sarcoma. Inoculation one and one-half months after castration gave 90 per cent of "takes" in the controls and 100 per cent in the castrated rats. The influence of castration was not very definite. Injection of a suspension of dogs' testicle, however, caused a retardation of the growth of the tumor. Injections of an autolysate of sarcoma in small amounts caused a retardation of growth, but larger doses were less energetic in their action. The same may be said for corpus luteum. Extirpation of the spleen seemed to augment the inoculability to sarcoma and favor its growth. Castration slightly attenuated the effect of splenectomy alone. Thyroid alimentation retarded the growth of tumors, and weak doses appeared to act better than strong. Pituitrin has shown no influence on the growth of tumors.—T. C. B.

INTERNAL SECRETIONS, Contributions to the pathology of—(Part II.) Nakamura (H.), Verhandl. d. jap. path. Gesellsch., 1919, ——, 41-43.

In the first part the author describes the effect of the ligation of both spermatic cords in rabbits killed 1, 2½, 4½ and 7½ months later, as follows: (1) A general increase in body fat which is most apparent after about 4½ months; (2) The interstitial fatty tissue of the thymus is reduced, the lymphatic cortical substance is increased, while the Hassal's corpuscles show no change in either size or number; (3) The thyroid is of the colloid type; (4) In the suprarenals there is a thickening of the cortical substance and an increase in the lipoid content of the cells, especially after 4½ months. The medullary substance is not increased, but after 7½ months shows a somewhat stronger chromaphil reaction; (5) There is also an increase in the chromophobe cells of the hypophysis.

In the second part he notes the following changes in the glands of internal secretion in persons of from 50 to 90 years of age: (1) Atrophy of the thymus and reduction in the size of the Hassal's corpuscles; (2) Variability in the follicular contents of the thyroid, deposition of lipoid and pigment in the follicular cells and increase in interstitial connective tissue; (3) Reduction in the suprarenal cortex and variability in its lipoid content; (4) The appearance of brown granular pigment in the posterior lobe of the hypophysis and the relative or absolute disappearance of eosinophile cells in the anterior lobe. In women the eosinophile cells are more numerous than in men.

The third and last part deals with death from suffocation in children in status thymicolymphaticus. It does not contain any new information.—E. V. C.

(INTERNAL SECRETIONS) Some remarks on the physiology of the ductless glands. Priestly (Henry), Med. J. Australia (Sydney), 1920 (i), 381-383.

A short review of the subject is given. No new data are included.—J. H. L.

(INTERNAL SECRETIONS) Mental deficiency and criminality. Schlapp (Max G.), Med. Rec. (N. Y.), 1920, **97**, 554-557.

The author divides mental defectives into three groups: (1) The traumatic type, in which there has been injury to the brain; (2) the formative type, in which the brain has not de-

veloped properly; (3) the functional type, "where there is a disturbance in the proportion of the different chemical factors in the surrounding medium from which the cells draw their necessary potential energy and activating substances, and therefore the cells do not react normally to stimulation." Schlapp believes a fair number of this latter group are caused by a disturbance of the internal secretions, and hopes that further study will permit more exact recognition of various types with consequent improvement under appropriate gland therapy. "In many of the cases examined at the Post-Graduate Hospital, chemical disturbance was found, and in more than half of these cases the cause was traced directly to certain of the internal secretory glands; and the encouraging part of it is that most of these people can be relieved if not cured." "Where the disturbance is of thyroid origin, methods have been fairly well worked out, and there has been some success with suprarenal unbalances, but the pituitary and other glands have not yet revealed their secrets."—H. L.

LIPODYSTROPHIA. Langmead (F.), Brit. J. Child. Dis. (Lond.), 1920, **17,** 33.

A case of a girl of seven years of age. The wasting was confined to the upper part of the body and ended at the level of the umbilicus. The face and neck were extremely wasted, the arms to a less extent, and the chest and trunk progressively less in a downward direction. The lower limbs were normal. The child was in general good health.—M. B. G.

(MAMMA) Homologous milk injection and mammary secretion during lactation (Eigenmilchinjection und Brustsekretion bei Wöchnerinnen). Lönne (Fr.), Zentralbl. f. Gyn. (Kiel), 1919, **43,** 908-915.

The injection under the nates of ½ cc. of milk from the breasts of the patient herself resulted in a marked increase in the secretory activity of the mammary glands in all of the six cases studied. Suggestion may play a rôle in the effect produced.—F. S. H.

(MONGOLISM) Two cases of Mongolian idiocy in the same family. Pardee (I. H.), J. Am. M. Ass. (Chicago), 1920, **74,** 94-95.

An interesting case report of two Mongolian idiots. The parents were Italians, the father 45 years of age, the mother 38 when the last child was born. These idiots were the young-

est in a family of eleven children. The other members of the family were normal. R. P., age 7 years, was born after prolonged labor, is undersized, has blepharitis; almond-shaped eyes; epicanthic folds; left external stabismus; thick lips; large protruding tongue with transverse fissures; broad, flat nose; soft, dry, hairless skin; hypotonic joints; oblique thumb and short little finger; undescended testicles, and no signs of the second dentition. His vocabulary is limited to single words. E. P., age 4 years, is very noisy, destructive and always busy. Physically he is the counterpart of his brother. The author discusses briefly the relation of the birth of Mongols to the period of the reproductive life of the mother. In this case the mother was of pronounced dyspituitary type, with nasal eyebrows, spacing of the incisors, obesity, frequent frontal headaches, and a history of diabetes in her mother. The children with their dry, smooth, hairless skin, small stature, prognathism, abnormal bony growths, and undescended testicles show definite signs which could be classed as polyglandular. For these reasons the author favors a possible endocrine factor in the development of Mongolian idiots, despite the fact that endocrine therapy has hitherto been unavailing.—F. C. P.

Death following OBESITY (Muerta consecutiva a obesidad). Marañon (G.), Real Acad. Nat. de Med. (Madrid), April 20th, 1918.

The case is reported of a woman of 29 years, who was actually a monster. Her height was 160 cm.; weight, 157 K.; bust measure, 130 cm.; neck, 44 cm.; arm, 51 cm.; thigh, 96 cm., and abdomen at the level of the navel, 150 cm. She began to take on flesh after becoming affected with syphilis, menstruation becoming suspended at the same time. The subject died suddenly. Autopsy showed the ovaries to be larger than normal, weighing 17 to 20 gms., and very hard. The microscope revealed sclerotic ovarian degeneration. The thyroids were small and sclerotic, and there was persistence of the thymus.—E. B.

Clinical comments concerning opotherapeutic treatment in gynecology and obstetrics (Comentarios clinicos al tratamiento opoterápico en ginecologia y obstetricia). Botin (F.), Revista españ. de Obst. and Ginec., Madrid, 1918, ——, ——.

The author dwells upon the importance of opotherapy in many processes having relation to gynecology and the necessity for detailed study of the subjects. Frequently, besides

ovarian disturbances, there intervene other endocrine gland disturbances, these latter calling for the application of combined opotherapy.—E. B.

(ORGANOTHERAPY) Treatment and management of the neurasthenic individual. Neu (C. F.), Med. Rec. (N. Y.), 1920, **97,** 341-346.

The author devotes a paragraph to organotherapy in neurasthenia. He does not believe that much encouragement can be offered as yet for this type of therapeutics. "If it should be finally shown that certain disturbances of the functional interactivity of the internal glandular secretions are more or less responsible for producing the symptom-complex under consideration, and if it should be determined what brings about those disturbances of glandular activity, it may be possible that a therapy along these lines will be developed, but as yet very little is offered."—H. L.

OSTEOMALACIA: it is a rare or rather common disease. Dieffenbach (W. H.), Med. Rec. (N. Y.), 1920, **97,** 995-997.

"Nervous and mental depression during the climacteric frequently has, as a basis, calcium deficiency and osteomalacia is frequently associated with it. This points to gonad-ovarian deficiency." "As the parathyroid glands are now believed to preside over calcium metabolism as the thyroid presides over iodin metabolism, there is some reason to look for parathyroid abnormality in this disease. Adrenal deficiency is also believed to be a factor in many instances." The author advises trying organotherapy, particularly suprarenal, ovarian or testicular, and parathyroid, but presents no data demonstrating success by their use.—H. L.

OSTEOMALACIA, a study of the effects of certain organ extracts and oöphorectomy on the metabolism of calcium and magnesium. Freund (Hugo A.), & Lockwood (Bruce C.), Annals of Medicine (Hagerston, Md.), 1920, **1,** 67-76.

The authors record the valuable results of a study of a sort unfortunately relatively rare in the endocrine literature. A woman of 33 years, suffering from osteomalacia, was made the subject of a metabolic study under carefully controlled laboratory conditions. After a week's control period she was given successively desiccated thyroid gland in 5 grain doses, three times daily; pituitrin, 1 cc. hypodermatically, twice daily, and, finally, parathyroid extract in 1/10 grain doses—fre-

queney not stated. In each case the gland administration was continued for a week, with rest periods between experimental periods. Succeeding the parathyroid administration the ovaries were removed, both being found cystic. During each period of the study determinations were made of the calcium and magnesium intake and of the calcium and magnesium output in feces and urine. It was found that there was a marked calcium loss, as described by previous investigators in this disease. The magnesium showed a minute loss. In contrast with previously described cases, the greater amount of calcium was excreted in the urine. During the thyroid administration there was a negative calcium balance of 1.447 gms. as compared with a negative balance of 0.447 gms. during the control period. Similarly there was a negative balance of 0.327 gms. in case of magnesium during the thyroid period and of 0.027 gms. during the control period. During the pituitrin period the calcium balance was -2.604, and the magnesium balance -0.015. There was thus augmented calcium loss during both the thyroid and the pituitrin periods. The magnesium loss was more than ten times as great during the thyroid as during the normal period. During the pituitrin period there was little change in magnesium excretion. During the parathyroid period, on the other hand, there was a marked gain, both in calcium and magnesium, the balances being positive, 0.616 and 0.775 gms., respectively. After removal of the ovaries there was much greater loss of calcium and a slightly greater loss of magnesium than during any preceding period. The negative balance for calcium was 5.086 and for magnesium 0.291. The castration was not successful in arresting the disease, as is shown both by these figures and by the clinical condition of the patient a year later.—R. G. H.

(OVA) Grafts of the eggs of anura upon adults of the same species or upon adult urodeles (Greffes d'oeufs de batraciens anoures sur des adultes de mème espèces ou sur des batraciens urodelles adultes). Weber (A.), Compt. rend. Soc. de biol. (Paris), 1920, **83**, 891-892.

Not of endocrine interest.—T. C. B.

(OVARY) Effects of castration upon the automatic movements of the uterus in the guinea-pig (Effets de las castration sur les mouvements automatiques de l'utérus chez le cobaye). Athias (M.), J. Physiol. et de Path. Gén. (Paris), 1920, **18**, 731-743.

The uterus to be studied was removed from the body and preserved in a nutrient fluid. The automatic movements of

uteri from normal virgin guinea-pigs, before and after puberty, and of pregnant and non-pregnant uteri of normal animals that had had offspring were compared with the movements of uteri from similar animals which had had both ovaries removed at varying intervals before the experiment. Some of these latter were subcutaneously autografted with ovarian tissue a number of days after the preliminary operation. The observations of Fano, Bottazzi, etc., were confirmed, that the uterus possesses along with other muscular tissues a double contractile function, clonic and tonic. The clonic type is seen in the form of more or less marked automatic rhythmic contractions. The tonic function is revealed by oscillations of varying duration in the tone of the contracture. It was found that castration results in definite modifications of the motility of the uterus. These are evidenced by a gradual weakening and final disappearance of the involuntary contractions. The tonic function of the uterus, however, remains normal or is even increased. These modifications are attributed to the suppression of the internal secretion of the ovary. They are not seen in the animals that were grafted with ovarian tissue.
—L. G. K.

(OVARY) Deficiency of the internal sexual organs (Ontbreken der inwendige geslachtsorganen). Boshouwers (H.), Medisch Weekblad (Amsterdam), 1920, **27,** 109-110.

Description of a woman of 35 who never menstruated. She was of a male type (large hands and feet and weight of 174 cm.). The muscles were strongly developed. In the breasts no glandular tissue could be felt. The vagina was 3 cm. deep and ended blindly. Upon palpation by rectum no uterus or ovaries were felt. The author thinks of the possibility that the large hands and feet are caused by a hyperfunction of the hypophysis, the antagonist of which, the ovary, is lacking in this case.—J. K.

(OVARY) Hormones and menstruation. Burckhardt-Socin (O.) Corresp. Bl. f. Schweiz Ärtze (Basle), 1918, **48,** 1431-1435.

Ovarian extract is potent in so far as it contains substances derived from the corpus luteum. Two of these, "luteolipoid" and "lipamine," have been prepared in tabloid form: the first acts as a haemostatic, the other encourages the menstrual flow. The author claims valuable clinical results in their use in the relief of excessive bleeding, pain, and other menstrual disorders.—Physiol. Abst. **3,** 528.

(OVARY THYROID ADRENAL) Headache with mild endocrine disturbance. Garmendia (F. S.), Revista Médica del Uruguay (Montevideo), 1920, **23**, 57-61.

Garmendia reports two cases of headache for which thyroid insufficiency was evidently responsible, and which yielded to thyroid treatment. In another case, latent chronic suprarenal insufficiency was finally detected and under epinephrin treatment, supplemented by recalcification measures, the patient regained strength and the headaches disappeared. In his fourth case a young woman had violent headaches during the menstrual periods, with occasional milder headaches in the intervals, and menstruation was scanty and painful. Tachycardia, a soft pulse, and pains in the region of the ovaries confirmed the assumption of ovarian insufficiency, and under ovarian extract treatment there has been no return of the disturbances during the four months to date. The symptoms in the suprarenal case had been great weakness, frequent nausea, pains in the left hypochondrium, and intense and frequent headaches. Small patches of slight pigmentation were found in the axillae and at the waist. The headache in the thyroid cases was in the upper and front part of the head and lasted the whole day, the skin was dry, and the outer portion of the eyebrows was scant of hairs.—J. Am. M. Ass., **74**, 1357.

Influence of the OVARY on metabolism (Die Beeinflussung des Stoffwechsels durch das Ovarium). Guggisberg (H.), Zentrabl. f. Gyn. (Kiel), 1919, **43**, 561-564.

When 0.1 ccm. of a 1/1000 adrenalin solution is injected into normal women there occurs only a slight increase in the blood sugar. The injection of the same amount into women whose ovaries have been removed causes a marked rise of the blood sugar within half an hour. The same result was obtained in spayed rabbits. These results indicate to the author that the ovary plays a rôle in carbohydrate metabolism.—F. S. H.

(OVARY) Studies on the Graafian follicles (Estudio de la genesis y evolucion del foliculo de Graaf. I. Embryologia del foliculo de Graaf. II. Evolucion del foliculo de Graaf hasta su madurez). Guilera Molas (L. G.), Bol. de la Soc. Españ. de Biol. (Madrid), 1918, **8**, 246-286.

An interesting histological and physiological study impossible to abstract.—G. M.

OVARY, Clinical results of transplantation of— (Klinische Ergebnisse der Eierstocksüberpflangzung). Hartog, Deutsche med. Wchnschr. (Berlin), 1920, **46,** 784.

Technical details. Autotransplantation is generally followed by reappearance of menstruation. Often two or three years after the operation menstruation becomes irregular and ceases.—J. K.

(OVARY) The involuntary nervous system in pregnancy and treatment of toxicosis with ovary (Das vegetative Nervensystem in des Gravidität und die Ovarialtherapie der Toxikosen). Hofbauer, Deutsche med. Wchnschr. (Berlin), 1920, **46,** 758.

The sympathetic and parasympathetic nervous systems show during pregnancy an increased degree of irritability. This is caused, supposedly, by the increased function of hypophysis, thyroid and adrenals. In cases of hyperemesis during pregnancy the author saw good results of ovoglandol (doses, etc., are not given). During eclampsia ovoglandol may be tried to diminish blood pressure and to diminish the spasm of the blood vessels. The exudation diathesis and the inclination toward the formation of edema in pregnancy are also due to changes in the endocrine organ.—J. K.

(OVARY) Ovarian metrorrhagia and radiotherapy (Metrorragios ovariales y radioterapia). Macan (J.), Revista españ. de obst. y ginec. (Madrid), 1918, ——, ——.

In addition to metrorrhagia due to internal lesions there exists others which are exclusively due to disturbances of the ovarian functions. This gland possesses different hormones which mediate distinct functions. In the successive phases of the development of the corpus luteum, there are formed various lipoid substances which act in a characteristic manner. The young lutein cells contain "lipomins" or "lutamins" having properties stimulating congestive conditions and determining the modifications necessary to bring on menstruation. In the corpus luteum there are already developed "luteolipoid" substances possessing the property of inducing ischemia. To these is attributed the suppression of the menstrual flow during the period of gestation. When the corpus luteum is insufficient and fails of complete development, the "lipomins" persist but without forming the "ischemic" hormones, and therefore metrorrhagia occurs. The author recommends radiotherapy in these cases.—E. B.

(OVARY) Contribution to the clinical study of ovarian insufficiency (Contribución al estudio dela clinica de la insuficiencia ovárica). Marañón (G.), Revista españ. de obst. y ginec. (Madrid), 1917, ——, ——.

The ovary is a mixed gland having an exocrine function, ovulation, and another, the endocrine function. As regards the endocrine functions there exist three classes of hormones: (1) "Genital," elaborated by the corpus luteum, which actuates the genital life of the woman, affecting menstruation and conception; (2) "Sexual," which exert their influence upon the appearance and development of the primary and secondary sexual characters, probably engendered by the interstitial and folicular tissue, and (3) General, which act on the entire organism, affecting metabolism and the nervous system, principally the vegetative. Their origin is complex. The corpus luteum determines the structural changes necessary for menstruation, and equally for impregnation of the ovum, to the insufficiency of which it is possible to attribute inexplicable abortions, those not due to habitual causes, syphilis, etc. Other glands of internal secretion intervene in the physiology of the ovary, thyroid, hypophysis and suprarenal capsules. Considering these facts it becomes comprehensible how ovarian insufficiency may manifest itself in such different forms as: (1) Simple luteal insufficiency accompanied only by menstrual disturbances; (2) Total ovarian insufficiency in which in addition to the menstrual disturbances there is scant development of the primary and secondary sexual characters, tendency to obesity, local adiposity, trophoneuroses, headache, vasomotor disturbances, etc.; chlorosis and many cases of asthma have a hypovarian pathogeny; (3) Ovarian insufficiency accompanied by the reaction of other glands, thyroid-ovarian, suprarenal-ovarian, hypophyseal-ovarian and pluriglandular syndromes. In total ovarian insufficiency opotheapy ought almost always to be employed and in the combined syndromes ovarian with other glandular extracts. It is only when menstrual disturbances dominate that corpus luteum extract is employed. There exists ovarian hemorrhage due to the circumstance that the corpus luteum possesses different hormones according to the epoch of its development; some of these favor coagulation of the blood. This explains the paradox of the appearance of menorrhagia, which gives way to ovarian opotherapy.—E. B.

(OVARY THYROID) Two cases of catamenial angina (Sobre dos casos de angina catamenial). Martin Calderin (A.), Revista de med. y cirug. pract. (Madrid), 1918, ——, ——.

The author reports the history of two young women affected with thyroid-ovarian insufficiency. Coincident with the appearance of the menses, there appeared sudden attacks of streptococcic angina. This is a picture analagous to catamenial erysipelas, and undoubtedly is due to diminution of the organic defenses because of humoral disturbances which originate in endocrine insufficiency.—E. B.

(OVARY) The theory of ovulation and its relation to normal and pathological processes in the uterus with some remarks on hormone theory (Zur Lehre von der Ovulation und den mit ihr in Beziehungstehenden normalen und pathologischen Vorgängen am Uterus nebst Bemerkung zur Hormonlehre). Meyer (R.), Zentralbl. f. Gynak. (Leipzig), 1920, **44**, 473-479.

Complete data will be published in Archiv für Gynäkologie. This abstract of a larger article is of no immediate endocrine interest.—J. K.

Perturbations in the function of the OVARY and other endocrine glands and digestive disorders (Perturbaciones en el functionamiento del ovario y otras glándular endocrinas y alteraciones digestivas). Ygea Rodriguez (F.), Rev. españ. de obst. y ginec. (Madrid), 1917, ——, ——.

Observations of clinical cases frequently prove that digestive alterations are due to endocrine disorders. Among such cases was that of a young woman suffering from hyperthyroidism and gastric ulcer and, according to the physician who reported the case, ovarian disturbances, which brought on frequent and abundant menstruation. The hyperovarian syndrome of Dalché possesses very little clinical reality in those cases in which there is an absence of periodical menstrual disturbance and exaggerated flow. Modern knowledge of the physiology of the ovary and clinical observations lead more readily to the supposition that there exist in such cases an ovarian insufficiency and, more or less commonly associated therewith, hyperchlorhydria and gastric ulcer. Therefore the author with reason attributes the symptoms to vagatonia, inasmuch as the ovarian hormones tend to excite the tone of the vagus.—E. B.

(OVARY) The clinical signs of ovarian functional anomalies (Die klinischen Zeichen der Funktionsanomalien des Ovariums). Schröder (R.), Monatschr. f. Geburtsh. u. Gynaek. (Berlin), 1920, **51**, 217-232.

Constitutional factors may be responsible for excessive functioning of the ovaries, or the loss of inhibitory factors from other endocrine glands. Chronic metro-endometritis may develop as the consequence of long continued ovarian hyperfunctioning, but transient hyperfunction is usually a period of increased physical, mental and sexual vigor.

The etiology of ovarian insufficiency is remarkably many sided, yet such cases can be divided into two categories: those in which the cause of the insufficiency lies in the ovary itself,—primary insufficiency, and those due to an external harmful influence acting on the ovary,—secondary insufficiency. In the first group the author puts infantilism of all types, congenital and acquired. In the second group are put the various pathological growths affecting the ovary; the disturbances of internal secretion,—hyper-and hypo-thyroidism, adrenal and hypophyseal insufficiencies; cachexia of any type and acute and chronic intoxications arising from metabolic or nutritional disturbances; primary and secondary anemias; psychic disturbances and unknown causes arising at the climacteric; carbon dioxid intoxication from defective circulation; nervous or mental derangement; change of climate, and unknown causes.

If all these can be excluded, primary insufficiency of the ovaries may be assumed, and proper treatment instituted. Perverted ovarian functioning is manifested in irregular bleeding from the uterus from the persistence of ripe follicles without any corpus luteum stage. With cystic degeneration of the ovaries, the follicles do not ripen, but with this hemorrhagic metropathy the persistence of the follicles keeps the endometrium in a constant state of proliferation. Another anomaly for which perverted ovarian secretion is known to be responsible is the persisting corpus luteum. It may be so large as to simulate extra-uterine pregnancy.—F. S. H.

(OVARY) An ectopic ovarian cyst. Thompson (J. W.), Brit. M. J. (London), 1920 (i), 437.

Not of endocrine interest.—L. G. K.

A case of PSORIASIS with AMENORRHEA cured with ovarian therapy (Un caso di psoriasi generalizzata con amenorrea guarito con il trattamento opoterapico). Verrotti (G.), Riforma med. (Napoli), 1920, **36**, 321-322.

The patient whose case is reported had been ill of psoriasis and amenorrhea more than six years, and no treatment had given any lasting result. Finally, after a few months of

ovarian treatment the menstruation reappeared and the psoriasis was fully cured. Verrotti calls this psoriasis a toxidermia due to alterations of the utero-ovarian function and insists on autointoxication as one cause of the dermatoses.—G. V.

OVARY and symptoms of reduced function (Ovarium werking en de Z. G. uitvalsverschijnselen). Wesselink (D. G.), Neder. Maandschr v. Geneesk. (Leiden), 1920, **1**, 196-215.

In women suffering from menstrual disorders we must distinguish the complaint immediately before menstruation (which are due to hyperfunction of the ovaries) from the complaint during menstruation (which is due to a temporary cessation of the internal secretion of the ovary). These complaints are the same, but in lesser degree, as the complaints in the same person after castration. Therefore it is necessary in women with menstrual disorders who have to undergo gynaecological operations not to remove both ovaries if there is the slightest possibility of leaving at least one. Otherwise the menstrual complaints will return after castration in a permanent and more serious way.—J. K.

PANCREAS, Histogenesis of the islands of Langerhans in certain mammals (Sur l'histogénése des ilots des Langerhans chez certains mammiferes). Aron (M.), Compt. rend. Soc. de biol. (Paris), 1920, **83**, 631-634.

Of technical histological interest.

(PANCREAS) Life assurance and glycosuria. Cammidge (P. J.), Lancet (London), 1920, **i**, 836.

Advocates a determination of the blood sugar in cases of apparent glycosuria where there is doubt as to the nature of the reducing substance in the urine. Cases of pentosuria, levulosuria and pseudo-levulosuria show a normal blood sugar content, and after a test meal the percentage of sugar in the blood follows a normal curve indicating that the carbohydrate tolerance is not diminished in spite of the presence of "sugar" in the urine. The author places much more reliance on examinations of the blood than of the urine in the diagnosis and treatment of diabetes.—L. G. K.

(PANCREAS) Pancreatic dehydration in diabetic coma (La déshydration du pancréas dans le coma diabètique). Chauffard (A.) & Grigant (A.), Bull. et mem. Soc. med. d. Hôp. (Paris), 1919, 3. s., **43**, 939-942.

It would appear from the results published by these authors that the water content of the pancreas of an individual dying in diabetic coma was less than normal; even the spinal fluid was thick and syrupy, and the coefficient of dehydration in the pancreas was 170 per thousand. Since, however, the values are apparently based on but one normal and one pathological case, the ultimate decision should be withheld.—F. S. H.

PANCREAS, The diagnosis of disease of the—. Feldman (W. M.), Brit. M. J. (London), 1920 (**i**), 553-554.

The author states that in individuals who are normally sympatheticotonic the Loewi adrenalin mydriasis test for pancreatic insufficiency is of no value since such persons give a positive reaction in the absence of any pancreatic derangement. Other tests are suggested (Aschner's oculo-cardiac reflex and the respiratory cardiac reflex) as of value in the diagnosis of disease of the pancreas by detecting signs of a hyperactive sympathetic nervous system. All three of these reactions are of use only when the patient is known to be normally a vagotonic.—L. G. K.

(PANCREAS) Life assurance and glycosuria. Fox (R. H.), Lancet (London), 1920, **i**, 836. Also May (O.), ibid, 836-837.

These authors dissent from Williamson's article (see abstract elsewhere in this number) in that they believe that an applicant for life assurance in whom glycosuria has been found should not be told the nature of his affection but should be merely advised to consult his own physician. Exception is also taken to the severity of treatment recommended for cases of temporary glycosuria. Many such cases are said to be "nothing more than a functional derangement," and consequently acceptance by the insurance companies at ordinary rates is advised.—L. G. K.

PANCREAS, The Schornstein Lecture on the diagnosis of diseases of the—. Garrod (A. E.), Brit. M. J. (London), 1920, **i**, 459-464.

A considerable portion of the paper deals entirely with the external secretory functions of the pancreas. Loewi's adrenalin mydriasis test as a sign of pancreatic insufficiency is recommended as an aid in diagnosis. The absence of glycosuria is said to afford no argument against the presence of disease of the pancreas. The same may be said of lowered sugar tolerance which may be present in disturbances of other ductless glands. Cammidge's reaction is advocated as

an aid in detecting pancreatic derangements. The author emphasizes the fact that "practically every sign, symptom or test may fail at times, and that in each individual case we need to balance the quantity and quality of the evidence for and against a lesion of the pancreas." It is still true, as Wardell stated in 1871, that "no symptoms are pathognomic of pancreatic disease; an assemblage of symptoms points to the probability of its lesion."—L. G. K.

(PANCREAS) Proof of nuclear digestion and the diagnosis of pancreatic insufficiency (L'épreuve de la digestion des noyaux et la liagnostic de l'insuffisance pancréatique). Labbé (M.), Bull. et mem. Soc. med. d. hôp. (Paris), 1919, 3. s., **43,** 794-785.

Of no endocrine interest.—F. S. H.

(PANCREAS) Anaesthetics and diabetes mellitus. Leyton (O.), Lancet (London), 1920, **i,** 736.

The author emphasizes the fact that a general anesthetic may lead to the transformation of a comparatively slight case of diabetes into one of great severity. A diabetic who has been able to take a diet supplying sufficient energy to allow the individual to maintain his weight and to do a certain amount of manual labor finds that after a general anesthetic he can no longer remain sugar free on a diet which will permit him to retain his weight. Therefore only absolutely essential operations should be performed upon diabetics, and spinal anesthesia and local anesthesia should be adopted when possible. Nitrous oxide with oxygen is less likely to damage the patient than ether, and ether is less harmful than chloroform.—L. G. K.

(PANCREAS) Incipient diabetes mellitus. Mason (E. H.) & Sutherland (C. G.), Can. M. Ass. J. (Toronto), 1920, **10,** 657-660.

Four cases are reported in which a transient glycosuria was discovered during life insurance or other examinations. In no instance did the blood sugar follow a normal curve after administration of 100 grams of glucose on a fasting stomach. In one case the sugar in the blood reached 0.348 per cent, a figure frequently not exceeded in many outspoken cases of diabetes mellitus after a similar proceeding. The blood sugar reached its maximum concentration on the average in 1.3 hours. The fasting blood sugar averaged 0.131 per cent, and

this figure was again reached 2.8 hours after the ingestion of the glucose. Three of the cases showed a slight glycosuria. The glucose threshold in the kidneys, as estimated on the fall of the curve, averaged 0.192 per cent, being remarkably raised in two cases, 0.2 per cent and 0.226 per cent. In none of the four cases could any abnormality in kidney function be determined.—L. G. K.

(PANCREAS) The glycogen in diabetes following pancreatectomy (Les glycogéne dans les diabéte par extirpation du pancreas). Paulesco (N.), Compt. rend. Soc. de biol. (Paris), 1920, **83,** 562-565.

A recent hypothesis explains diabetes following pancreas extirpation by the fact that the liver and muscles have lost their power to fix glucose in the form of glycogen. It is desirable to know precisely whether the incapacity of the tissues to form glycogen is absolute or relative; whether it is the direct effect of pancreatic insufficiency or a phenomenon that is secondary and contingent. The experiments consisted of total ablation of the pancreas; at the same time a lobe of the liver was removed to determine the quantity of glycogen in the beginning of the experiment and finally the autopsies were performed. In one set of experiments the animal was starved; in the other it was fed on various sugars. The conclusion is that after total ablation of the pancreas the ability of the liver to retain glycogen is considerably reduced, but not annihilated. The same can be said for muscle. The power of the myocardium to fix glycogen remains normal and persists until death sixteen days after the operation. The glycogenic incapacity is relative,—a contingent phenomenon,—and not the cause of diabetes.—T. C. B.

(PANCREAS) Pancreatic infantilism. Sainz de los Terreros (C.), Siglo Med. (Madrid), 1920, **67,** 221-223; Abstr. J. Am. M. Ass. (Chicago), 1920, **75,** 138.

The author refers to backward growth from insufficiency of the pancreas. The literature records few instances of this, but he has encountered it in a number of children. The pancreatic insufficiency does not entail diabetes in children, although certain features of the metabolism resemble those of diabetes in adults and transient alimentary glycosuria is common in children. His experience has convinced him that the pancreas has three hormones in all probability, one serving for carbohydrate metabolism, one for the interglandular control of growth and development, and the third forming

the active element in the pancreatic juice. In children, insufficiency of the two last mentioned hormones will check normal digestion and also check normal growth, while the carbohydrate metabolism may proceed normally or with only minimal glycosuria and acetonuria. A child with pancreatic insufficiency begins to lose weight; acetone and preacetone bodies are thrown off in the urine and the thyroid, freed from the pancreatic hormone, functions to excess. There is usually a tendency to adenoids, pathologic tonsils, mononucleosis and often leucopenia; the resistance is low and the child contracts disease easily.—M. B. G.

(PANCREAS) The paranucleus of the pancreatic cell with reference to the work of Saguchi (Le paranucléus de la cellule pancréatique a propos d'un travail de Saguchi). Shaves (P. R.), Compt. rend. Soc. de biol. (Paris), 1920, **83**, 881-884.

Of histological interest.—T. C. B.

(PANCREAS) Life assurance and glycosuria. Williamson (R. T.), Lancet (London), 1920, **i**, 708-711; 934.

The author found a family history of diabetes in 22.4 per cent of 500 cases of diabetes while in a control series of 50 non-diabetic patients no family history of diabetes was obtained. He is of the opinion that a history of diabetes in one member of the family should not be regarded as requiring an extra charge for life insurance. However, a minimum extra charge is advised where two or more near relatives (brothers, sisters, parents) give a history of the disease.

If the urine of the applicant for insurance causes reduction of Fehling's solution and other symptoms of diabetes are present the case should be permanently rejected without further consideration. If there are no symptoms of diabetes, but Fehling's solution (or some modification) is reduced definitely, the case should be rejected, temporarily at least. Repeated examinations may be made to determine whether the reducing substance is sugar or some other substance. If the reduction of Fehling's solution is indefinite, before rejecting the case confirmatory tests for sugar should be made at once. If the reduction is not due to sugar the case may usually be accepted. The phenyl-hydrazin and fermentation tests are advised as confirmatory tests for glucose. If glycosuria is detected once only in several examinations of urine passed in the latter part of the day, and the sugar tolerance is not found to be lowered the case may be accepted with an

extra charge. However, if the sugar tolerance is diminished or if sugar is detected more than once rejection is advised. The author is also of the opinion that the examining physician should acquaint the proposer with the cause of his rejection and inform him of the exact significance of the glycosuria and of the importance of seeking treatment. It is essential that the patient be not alarmed as sometimes "a fear of diabetes," a neurosis similar to "sypilophobia" develops.

In a second paper the author defends his position that applicants for life assurance suffering from intermittent or temporary glycosuria should be informed by the examining physician of the nature of their ailment.—L. G. K.

PANCREATIC INSUFFICIENCY, Notes on a case of—. Symes (J. O.), Lancet (Lond.), 1920, (i), 494-495.

Not of endocrine interest.—L. G. K.

(PARATHYROID) The ammonia content of the blood and the neutrality regulation in epilepsy (Fortsatte Undersögelser over Neutraliteteregulation ved genuin Epilepsi). Bisgaard (A.) & Növig (P.), Hospitalstidende (Copenhagen), 1920, **63,** 49-62; Abst. Med. Sc. Abst. & Rev., **2,** 295.

The authors made about 2,000 blood examinations in 16 epileptics and a few normal controls. They found that blood ammonia varied in the epileptics from 0 to 1.42 mg. N. per 100 c.c., whereas the normal ranges is taken as 0.3 to 0.4 mg. The higher figures were obtained with regularity before an attack or a "psychic equivalent," while low values obtained after the attack. The urea content of the blood in epilepsy showed little deviation from the normal. The writers then compare the metabolism (calcium metabolism, as shown by the condition of the enamel, protein-metabolism, and NH_3 metabolism) characteristic of the three conditions, hypoparathyroidism in animals, tetany, and epilepsy, and they find striking uniformity in all. The most important difference is the absence in epilepsy of spasmophilic reactions which are common to hypoparathyroidism and tetany. The writers conclude that their investigations strengthen the view that genuine epilepsy is associated with hypo-function of the parathyroids. The recognition of a parathyroid epilepsy as a disease sui generis may also be followed by a subdivision of this disease according as the ordinary cases differ. Other details are given in the abstract cited.—R. G. H.

(PARATHYROIDS) Study of tetany in the adult incident to parathyroid apoplexy (Étude sur la tetanie de l'adulte par apoplexie paratyroidienne). Cordier (Mme. V.), Ann d. Méd. (Paris), 1920, **7**, 346-360.

A detailed report of a case of tetany in a man of 41 years with autopsy findings of a hematoma in the tracheo-thyroid region which had destroyed the right parathyroids, while the left parathyroids were hemorrhagic. The study of the progress of the disorder indicated that acidosis is an important symptom of tetany in the adult, although it was impossible to conclude that it is the basis. Opotherapy gave real relief in the earlier stages of the illness, but was ultimately unavailing. Tetany in the adult is briefly divided into five classes: (1) Surgical tetany; (2) Tetany in women attributable to an activity of the ovarian secretion on the parathyroids; (3) Tetanies of digestive origin in which possibly a particular kind of acidosis may play a part; (4) Tetany induced by infectious processes in the parathyroids; (5) Localized tetanies which are allocated to an endocrine insufficiency.—F. S. H.

(PARATHYROID) Tetany in the etiology of cataract (La tetania en la etiologia delas cataractas). Garrahan (J. P. & Belgeri (F.); Prensa med. argent. (Buenos Aires), 1920, **6**, 305.

The case is presented of a little girl four years of age who had suffered from convulsive attacks from her first to third years. She manifested hyperactive patellar reflexes, slight Chvostek's sign, hyperexcitability of the external popliteal nerve to mechanical stimulation and positive Erb's sign. She also had a zonular cataract. The authors believe that the cataract is probably to be ascribed to "latent tetany."
—B. A. H.

PARATHYROID transplantation, Data on the value of— (Erfahrungen über den Wert der Epithelkörperüberpflanzung bei postoperativer Tetanie). Jaeger (H.), Zentralbl. f. Chir. (Leipzig), 1920, **47**, 565-569.

Two cases were treated with transplantation with only very temporary success. In these cases administration of calcium gave no success, either. In some other cases some good effect was seen from calcium lactate.—J. K.

PARATHYROID immune bodies, On the Formation of—. Kishi (Isami), Tokyo Igakkwai, 1920, **34**, ——, (No. 9).

The author has attempted to make a serum for use in parathyroid tetany. He found that the serum of rabbits immunized against horse's parathyroid does contain a true parathyroid antibody which, however, lacks specificity, since it works equally well against the thyroid, pineal, hypophysis, suprarenal and lymph glands of the horse.—E. V. C.

(PARATHYROID) The importance of vagal and splanchnic afferent impulses on the onset and course of tetania parathyropriva. Palmer (W. L.), Am. J. Physiol. (Balt.), 1920, **52,** 581-590.

The great frequency with which tetany and gastro-intestinal disorders are associated clinically, led the author to think that afferent impulses reaching the central nervous system through the splanchnics and vagi might have some influence on the onset and course of parathyroid tetany. Two methods of procedure were followed. The first consisted in the determination of the effect of double vagotomy and splanchnectomy, and the second in the determination of the effect of gastro-intestinal irritation by means of croton oil. The technic of the operation and the results are given in detail. The conclusions drawn from the results obtained are, that neither double vagotomy and splanchnectomy, nor gastro-intestinal irritation have any influence on the onset and course of tetania parathyropriva.—T. C. B.

(PARATHYROID) Studies in the metabolic changes in experimental tetany. Togawa (Tokuji), (Tokyo), J. Lab. & Clin. M. (St. Louis), 1920, **5,** 299-306.

Togawa studied in eleven experimental young dogs and four controls the following: CO_2—combining power of the blood plasma, by the Van Slyke-Cullen method; the antitryptic power of the serum, by the Bergmann and Meyers methods; the non-protein nitrogen content of the serum, by Folin and Denis' methods. It was found that after parathyroidectomy (plus thyroidectomy) in dogs showing typical tetanic symptoms, a condition of acidosis always resulted, and the antitryptic power and the non-protein nitrogen content of the serum were usually increased. In cases, however, in which tetany did not occur, acidosis was not found. On the contrary a slight alkalosis was sometimes observed and the antitryptic power and the non-protein nitrogen remained practically unchanged.—R. G. H.

(PAROTID GLAND) Pellagra outbreak in Egypt. Enright (J. I.), Lancet (Lond.), 1920, (**i**), 998-1003.

From a study of pellagra among German prisoners of war, the conclusion is drawn that deficient diet or deficient digestion of the diet cannot be an important etiological factor. The food provided was abundant and varied. Parotitis was frequently an associated condition, and the suggestion is thrown out that the parotid gland forms an internal secretion which is required for protein utilization.—Physiol. Abst., **5,** 187.

(PINEAL) Comments on the function and clinical uses of the pineal gland. Berkeley (W. N.), Med. Rec. (N. Y.), 1920, **98,** 12-14.

There is now a recognized "pineal syndrome"—signs of cerebral tumor in the region of the corpora quadrigemina, concurrent with abnormal growth of the body, early appearance of axillary and pubic hair and remarkable sexual and mental precocity. The author in 1913 reported interesting experiments in feeding pineal gland to backward children with encouraging results in advancing the mental age. This work was confirmed and amplified by McCord. Horrax and Dandy obtained contradictory results from extirpation of the gland. The author inclines to doubt the reliability of surgical experiments because of the profound brain trauma incidental to the operation. Berkeley has continued his feeding of pineal glands to children (over long periods of time) with gratifying results. He calls attention to the advisability of combining pituitary, testis (or ovary) and thyroid with pineal gland when evidences of hypofunction of one or other of these glands is noticed. The gland preparation must be fresh and obtained from some well known and reliable source. Berkeley has also used pineal gland feeding in premature decay of the mental powers in old people and found that it quickens the slowed down mental processes, improves the memory and produces a remarkable cheerfulness and sense of well being. Finally, the author refers to Timmie's recent article in which he indicates a belief that progressive muscular dystrophy is of pineal origin.—H. L.

(PINEAL) On the nature of the epiphyseal cells (Sobre la naturaleza de las cellutas epifisarias). Hortega (Del R.), Bol. de la Soc. Españ. de Biol., Jan., 1917.

Histological study of the epiphyseal (pineal) gland which is considered a glio-epithelial organ, it not being possible to mark the limits between the epithelial and neurological elements.—G. M.

The PINEAL body; its structure, function and diseases. Jelliffe (S. E.), N. Y. Med. J. (N. Y.), 1920, **111**, 235-240; 269-275.

The pineal body may be considered as an independent organ certain parts of which have undergone a retrogressive evolution, while other parts have persisted and are undergoing progressive evolution. The lipoid material of the pineal body is related to visual purple of the photoreceptors of higher forms and is found in other forms in the pineal complex. This lipoid may be considered as an active transforming material for light energies. Alterations of the pineal structure can induce characteristic disease syndromes both as reactions due primarily to alterations of the gland itself or as syndromes due in part to the former, or to interference of functions of contiguous structures from pressure and extension of new growths. The article includes a general summary of the morphology, physiology and pathological physiology of the gland.—H. W.

(PINEAL) Pubertas praecox. Wiesenthal, Wiener klin. Wchnschr., 1920, **33**, 549.

Description of a boy of 20 months with development of penis as in a boy of 15 years, pigmentation of penis and erections. The voice is deep and the length of the body is as in a boy of 5 years. Upon radioscopy the ossification of the bones proved to be as in a boy of 12. There are no symptoms of brain tumor. The testicles are very small. The intelligence is normal. The cause of the condition has not been detected.
—J. K.

(PLACENTA) Cytological studies on the human placenta and decidua with special reference to their internal secretory activity. Fujimura (G.), Tokyo Igakkwai, 1919, **33**, 15.

The author obtained material from 43 cases in many stages of pregnancy and studied it by means of the newer methods of technique designed to show the plastosomes (mitochondria). He draws a close analogy between the different cells of the placenta and those of other glands like the pancreas, suprarenal and so forth. He is of the opinion that the secretion is formed from the mitochondria, which change first into lipoid granules and then into droplets of more fluid nature which appear in the preparations in the form of uncolored vacuoles. He claims also to have determined the approximate time at which the different types of cells produce their various secretions: (1) The cells of the syncytium, from the

beginning of pregnancy to the end of the fourth month, being most apparent in the second and third months; (2) Langhans cells to the sixth or seventh month; (3) Zottenstroma cells from the end of the first month to the seventh month; (4) Small decidua cells from the end of the first month to the seventh month, and large decidua cells from the second to the sixth month. The paper is beautifully illustrated with lithographic plates and the extensive literature is carefully reviewed.—E. V. C.

(PLACENTA) Histogenetic and histophysiologic studies on the placenta (in the mouse). Ohashi (Y.), Tokyo Igakkwai, 1920, **34**, —— (No. 10).

This is a rather extensive contribution published in two numbers of the journal. The author divides his description into three stages, viz.: (1) Before placenta formation; (2) Placenta formation, and (3) After placenta formation. Special attention is paid to the origin and distribution of glycogen in the placenta, but comparatively little is said regarding the formation of internal secretions by the placental cells.
—E. V. C.

POLYURIA from cerebral piqure in dogs with denervated kidneys (Poliura por pinchazo cerebral en perros con riñones desnervados). Houssay (B. A.) & Carulla (J. E.), Soc. de Biol. de Buenos Aires, June 10, 1920.

Four cases were reported.—B. A. H.

POLYURIA from cerebral piqure in the dog (Poliura por pinchazo en el perro). Houssay (B. A.), Carrula (J. E.) & Romaña (L.), Soc. de Biol. de Buenos Aires, June 10, 1920.

The piqure was made by means of the cautery in a zone which was included between the optic chiasma and the protuberance. In some, but not all cases, this produced a marked polyuria. Similar polyuria was never observed in case the piqure fell outside the zone described. The polyuria so produced is primary; it is not due to polydipsia, vascular hypertension or glycosuria. The polyuria which follows hypophysectomy may be due, perhaps, to the cerebral piqure involved in the operation.—B. A. H.

PROSTATE, The internal secretion of the—and its relation to the testes (La sécrétion interne de la prostate et ses rapports avec les testicules). Bogoslovsky (G.) & Korentchev-

sky (V.), Compt. rend. Soc. de biol. (Paris), 1920, **83**, 718-719.

Observations were made on eight dogs, two normal and six castrated. The normal equilibrium of exchange was established and the experiment divided into three periods. First, a period of three days for establishing the normal gaseous and nitrogen exchange. Second, a two or three-day period during which intravenous injections of emulsion of prostate, or of testicle, or both, were made. Third, a control period of one to three days. The results permit the following conclusions. Normal dogs show a slight increase of N exchange and diuresis under the influence of injections of prostate. In castrated dogs, the phenomenon is more accentuated—8 to 10 per cent. The simultaneous injection of prostate and testicle causes an augmentation of N up to 17 per cent, and of diuresis to 25 per cent. During the first four hours the N augmentation may be as much as 40 per cent and the diuresis 80 to 90 per cent. The prostate constitutes a powerful stimulant to the internal secretion of the testicles. The internal secretion of the testicles exercises a stimulating influence on the exchanges of protein substances especially.—T. C. B.

(PROSTATE) Loss of the specific secretion of cells cultivated in vitro (Perte de la sécrétion spécifique des cellules cultivées in vitro). Champy (Ch.), Compt. rend. Soc. de biol. (Paris), 1920, **83**, 842-843.

An attempt to ascertain if the properties of cultivated tissues are lost at the time of disappearance of the cytological characters. The prostate of the guinea pig was used, since the action of the ferment on the contents of the seminal vesicles can be clearly seen with small quantities of material. Fragments of the size used for culture give, when placed in vesicular fluid, a characteristic opaque appearance. Fragments placed in the ice chest for three or four days give the reaction unweakened; but if placed on plasma the reaction is lost by the fourth day. Histological controls show that the epithelium of the prostatic tubes survive, but give place to cicatrization at the surface as in other cultures; but it loses the particular characters of the normal prostate. The cells contain no characteristic secretion grains. There is, then, a correlation between the loss of differentiation and the disappearance of the characteristic secretion.

(SECRETIN) Action of acetone extracts of duodenal mucosa upon arterial pressure and upon the pancreas (Acció dels

extrets acetonics de mucosa duodenal sobre la pressió arterial i sobre del páncreas). Cervera (L.), Treballs de la Societat de Biologie, Barcelona, 1918, **6**, 19-21.

Extracts of duodenal mucosa made with acétone were compared with those made with acidulated saline solution as regards their effects upon blood pressure and pancreatic secretion. The acetone extracts were found to be somewhat less active but to produce a marked acceleration of pancreatic flow with no more than 10 mm. reduction of blood pressure. Hence secretin is not identical with Popielski's vasodilatin. Cervera suggests that the secretin acts on a "receptor substance" as postulated by Langley.—R. G. H.

(SECRETIN) Role of bile in the formation of secretin (Paper de la bilis en la formació de la secretina duodenal). Cervera (L.), Treballs de la Societat de Biologia, Barcelona, 1918, **6**, 22-23.

In view of the fact that secretin is supposedly elaborated normally in the duodenal mucosa in the presence of bile, Cervera investigated whether this latter substance plays any significant part in secretin formation. For a period of five days the bile was removed through a fistula, the loss of alkali being compensated for by the administration of sodium bicarbonate. At the end of the experimental period the duodenal mucosa was extracted in the classic manner and tested for its secretin content. The exclusion of bile from the duodenum had made no appreciable difference in the secretin formation.
—R. G. H.

Influence of SEX at different ages on the gravity of influenza (Influence du sexe aux différents ages sur la gravité de la grippe). Apert & Flipo, Bull. et mem. Soc. med. d. Hôp. (Paris), 1920, 3. s., **44**, 321-324.

A statistical presentation tending to show that grippe is of more severe effect when attacking females than the male.
—F. S. H.

SEX, Consideration of—in pediatrics (La considération du sexe en médicine infantile). Apert (E.), Bull. et mem. Soc. med. d. Hôp. (Paris), 1920, 3. s., **44**, 326-331.

From infancy on it is necessary to take into account in medical treatment the influence of sex. Disregard of the differences of the two sexes in planning hygienic and therapeutic measures is a grave error.—F. S. H.

Influence of SEX on the frequency of whooping cough (Influence du sexe sur la fréquence de la coqueluche). Apert (E.) & Cambessédès, Bull. et mem. soc. Med. d. Hôp. (Paris), 1920, 3. s., **44**, 324-326.

In France as in other countries, whooping cough is more frequent in females than in males.—F. S. H.

SPASMOPHILIA of older children (Die Spasmophille der älteren Kinder). Stneeman (H. A.), Jahrb. f. Kinderh. (Berlin), 1916, **86**, 43.

The author thinks that the glands of internal secretion may have a role in this disorder.—C. H. G.

SPASMOPHILIA, Experimental studies on the pathogenesis of— (Experimentelle Beiträge zur Pathogenese der Spasmophilie). Resch (A.), Jahrb. f. Kinderh. (Berlin), 1917, **86**, 294.

Resch studied the effect of B-iminazolylethylamine, para-oxyphenylethylamine, ethylamine, tenosin, choline and hypophysin upon the galvanic excitability of the peripheral nerves in the rabbit. Para-oxyphenylethylamine in subcutaneous doses of 0.05 gm. daily for a period of ten days and hypophysin in quantities of 1 cc. over a like period, increased the galvanic excitability of the sciatic nerve. Tenosin was inactive, while the others increased the nervous threshold. In a long theoretical discussion the author considers the possible rôle of soluble toxic proteinogenic amines of either endocrine or alimentary origin in the spasmophilic syndrome.—C. H. G.

Familial SPLENOMEGALY (Über familiäre Splenomegalie). De Lange (C). & Schippers (J. C.), Jahrb. f. Kinderh. (Berlin), 1917, **86**, 459.

Also reported in Amer. J. Dis. Child., 1918, **15**, 249, and abstracted in Endocrin., 1918, **2**, 192.—C. H. G.

(SPLEEN) Action of splenic extracts on smooth muscle. Preparation and nature of the active principle (Action des extraits de rate sur les organes á fibres musculaires lisses. Préparation et nature du principe actif). Stern (L.) & Rothlin (E.), J. de physiol. et de path. gén. (Paris), 1920, **18**, 753-780.

Hot or cold water extracts of the spleens of various animals contain a substance, "liénine," capable of causing con-

Pages 686 and 687: Reading matter on these pages is transposed.

sont-elles sous la dépendence des glandes génitales)? Mercier (L.), Compt. rend. Soc. de biol. (Paris), 1920, **83,** 470-471.

Mercier has observed that the secretion of the salivary glands of the male panorpa plays the role of an excitant to the female at the moment of copulation, and this gives rise to the idea that there may be a relation between these glands and the testes. The salivary glands attain a complete functional state at the moment when spermatogenic activity is finished, and it remains to see if the sexual dimorphism is not "en rapport" with the more or less precocious evolution of the genital glands.—T. C. B.

(TESTICLE) Treatment of eunuchoidism (Behandlung des Eunuchoidismus). Lichtenstern, München. med. Wchnschr., 1920, **67,** 620.

A young man of 20 was castrated for tuberculosis of both testicles. Eunuchoidism developed. It was cured by transplantation of a testicle of the father of the patient.—J. K.

TESTICLE transplantation, Influence of—on sexual life (Ueber die Beeinflussung des Geschlechtslebens durch freie Hodenüberpflauzung). Muhsam (R.), Deutsche med. Wchnschr. (Berlin), 1920, **46,** 823-825.

The author made testicular transplants in three patients. One of these had been castrated for tuberculosis of both testicles. One was suffering from bisexuality, while the third was homosexual. From the last patient one of the testicles was removed preceding the transplantation. In all cases the effect was splendid.—J. K.

(THYMUS) Report of a case of malignant thymoma with necropsy. Foot (N. C.), Am. J. Dis. Child. (Chicago), 1920, **20,** 1-14.

Report of a case in a child, male, aged 9 years, who gave a negative history until one month previously, at which time he began to complain of inspiratory dyspnea and inability to lie flat in bed because of marked orthopnea. Two weeks prior to admission to the hospital his mother noticed swollen veins at the base of the neck just above the clavicle. He had occasional fits of gagging and coughing, which would awaken him at night, but no cyanosis. Physical examination showed dullness on both sides of the sternum from the first to the fifth rib; breath sounds and voice sounds were increased. Radioscopy showed a large mediastinal tumor occupying the

traction of smooth muscle. This is said to be the active principle of the organ. Details of the method of preparation are given. Liénine is soluble in water and in alcohol, and insoluble in ether, chloroform, toluol, petroleum ether and benzol. It is thermostable and resists the action of acids and enzymes. It dialyses readily and does not give the biuret or Fehling's reaction. It is a nitrogenous substance, probably an amine. It acts directly on the smooth muscle fibre and not on the myoneural junction or nerve ending, thus resembling histamine in its site of action. (Seen also Endocrin., 1920, **4**, 260.)—L. G. K.

Splenomegaly and INFANTILISM (Esplenomegalia e infantilismo). Jiminez Adna (L.), Siglo med. (Madrid), 1917, ——, ——, (Sept.).

The author reports a case of infantilism with very marked splenomegaly due to Banti's disease. Other various cases are to be found in medical literature in which infantilism was accompanied by splenomegaly due to Banti's disease, hemolytic icterus, etc. These cases may properly be included in Pende's group of exo-endocrine syndromes.—G. M.

(TESTES) Experimental diabetes insipidus and genital atrophy (Diabétes insipide expérimental et atrophie genitale). Camus (J.) & Roussy (G.), Compt. rend. Soc. de biol. (Paris), 1920, **83**, 901-902.

Description of the genital organs of one of the dogs with permanent diabetes insipidus previously reported. The dog weighed 26 kgs., but had a small penis for its size, with small testicles badly descended, and poorly distinguishable scrotum. This may be due to injury of the hypophysis, but it is not impossible that the lesion of the opto-peduncular space of the brain may have caused the genital atrophy as well as the diabetes.—T. C. B.

(TESTES) The seasonal cycle of the testicle of the blind worm orvet (Les cycle saisonnier du testicule des l'orvet). 'Dalq (A.), Compt. rend. Soc. de biol. (Paris), 1920, **83**, 820-821.

A histological description of the male genital glands in the orvet, in different months of the year.—T. C. B.

(TESTES) Are the salivary glands of Panorpa dependent upon the genital glands (Les glandes salivaires des Panorpes

upper central part of the chest anterior to the great vessels. At the operation the patient took the ether well until partially anesthetized, but as anesthesia became more profound he grew markedly cyanotic. The ether was stopped and the usual restoratives administered with a resulting return of his color to the normal and his heart in apparently good condition. He, however, never regained consciousness and one-half hour after starting the ether he suddenly became very pale and respiration and heart stopped abruptly.

Necropsy showed a very hard lobulated tumor occupying chiefly the anterior mediastinum, lying just behind the sternum but not infiltrating the bone. It showed metastasis by direct lymphatic extension with three possible minor metastases at a distance. It did not penetrate the lung nor other neighboring organs much more deeply than their serous coverings or sacs. It was composed chiefly of small cells resembling microlymphocytes, but having vesicular nuclei, acidophil cytoplasm and tending very slightly to anastomose with one another by means of slender processes. This applied only to a decided minority of their number, the majority being discrete. The rest of the tumor was chiefly cartilagenous connective tissue. Neighboring lymph nodes, while they showed a few discrete tumor cells in their sinuses, were usually not incorporated in the tumor mass. The author feels that the tumor was of thymic origin and different from the lymphosarcomas that originate in lymphnodes. He gives a short review of the literature.—M. B. G.

(THYMUS) Primary malignant tumor of the anterior mediastinum. Lymphadenoma of thymic origin (Tumeur maligne primitive du médiastin antérieur. Lymphadénome d'origine thymique.) Dandy (Ch.) & Piédelièvre (R.), Bull. et mem. Soc. med. d. hôp. (Paris), 1920, 3. s., **44**, 867-876.

The case is reported of a mediastinal tumor in a man of 40, which developed at the expense of the thymus. There were symptoms of obstruction of the superior vena cava. Under the microscope the tumor appeared as a lymphadenoma. In spite of the absence of corpuscles of Hassal, the authors insist that the tumor was of thymic origin.—R. G. H.

THYMUS, The normal weight of— (Ueber das normale Gewicht der Thymusdrüse). Ishibashi (Matsuzo), Verhandl. d. japan. path. Gesellsch. (Tokyo), 1916, **6**, 19-20.

The thymus glands from 421 autopsies in the Pathological Institute of the Imperial University at Tokyo were weighed

and the weights tabulated according to age from birth to 80 years. The smallest average weight was noted at 6 months (5.30 gms.). The highest weight fell at 14-15 years (16.28 gms.). From this age there was a gradual decline to about 10 gms. at 30 years and finally to 6.5 gms. at 70. The article affords valuable data for those interested in the anatomical constants of the thymus.—R. G. H.

THYMUS death in children (Contribucion casuistica al estudio dela muerte timica en los niños). Palancar (J.) & de Arcaute (L. R.), Archivos Españoles de Pediatria (Madrid), 1918, **2**, 208-241.

This article describes the sudden death of two children, one of 10 months and the other of 4. Autopsy revealed nothing abnormal except exceeding hypertrophy of the thymus, which weighed 30 and 28 gms., respectively. In the case of the younger child, histological study of the thymus showed extensive development and abundance of the corpuscles of Hassall, which indicates to the authors that in hypertrophy of the thymus there is glandular hyperfunction. The authors also take into account the different pathogenic theories of thymus death, hypertensive coagulative, and toxic action on the myocardium (Thymusherz of the Germans) and equally, the part which the suprarenals play (chromaffin aplasia in status thymicus). In these cases there was no alteration in the chromaphil system. The necropsy observations favor the view of Popper and Fishl, who attribute thmyus death to coagulation in the heart and vessels which impedes filling of the aorta.—E. B.

(THYMUS THYROID) Contribution to the physiology of the glands. 42. Studies of the function of the thymus and the thyroid as shown by the respiratory metabolism at normal and increased external temperatures (Beiträge zur Physiologie der Drüsen. 42 Mitteilung. Untersuchungen über die Funktion der Thymus und der Schilddrüse, geprüft am Verhalten des respiratorischen Stoffwechsels bei normaler und erhöhter Aussentemperatur). Ruchti (E.), Biochem. Ztschr. (Berlin), 1920, **105**, 1-42.

Working in Asher's laboratory with thyroidectomized and thymectomized rabbits, Ruchti found that these animals not only stand the removal of these glands but also are good subjects for studies of respiratory exchange. Thyroidectomy causes a marked decrease in the carbon-dioxide and water output, while thymectomy has but little effect, which, however, is

in the same direction. Simultaneous removal of both glands is followed by a great decrease in carbon-dioxide and water output and thyroidectomy after thymectomy has the same result, the lower values remaining constant. When thymectomy is done after thyroidectomy no lower results are obtained; but here, too, the values fail to rise at a later period as occurs when the thyroid alone is removed. These facts seem to be the first experimental proof that the thymus and thyroid stand in opposite functional roles. At higher external temperatures (33° C.) the operated animals show a lesser respiration rate than do the normals.—F. S. H.

THYMUS. Changes of the—in experimental infections of mice (Die Veränderunug der Thymus bei der experimentellen Infektion der Mäuse). Takeuchi (Kiyoshi), Verhandl. d. japan. path. Gesellsch. (Tokyo), 1916, **6**, 17.

Fifty-seven mice were infected with Bacillus coli communis. The ratio of the thymus weight to body weight was studied. This ratio increased at first, reaching its highest value in 50-70 hours. This "hyperplastic stage" was followed by an "atrophic stage." In the hyperplastic stage the gland appeared in the gross grayish-white, translucent and edematous. The microscopic findings were as follows:

Hyperplastic stage—	Atrophic stage—
Boundaries of cortex and medulla obscure	Boundaries still more obscure
Small cells in medulla markedly increased	Small cells almost lacking, leaving only reticular tissue and Hassal's corpuscles
Reticulated tissue, no notable change	Augmented growth; many multinuclear giant cells apparent
Eosinophile cells, not increased.	Not increased as in human subjects
Hassal's corpuscles, no noteworthy changes	No changes
Connective tissue increased	Increased.

—R. G. H.

(THYROID) Syphilis and Graves' disease. Editorial note, Med. Rec. (N. Y.), 1920, **97**, 698.

Levy-Franckel, Pierre Marie, Gaucher, Sainton and Schulman have called attention to the surprising frequency of syph-

ilitic Graves' disease. Iodides that are contraindicated in ordinary exophthalmic goitre are beneficial in the luetic variety.
—H. L.

Thyroid and heat regulation (Schilddrüse und Wärmeregulation). Adler (L.), Med. Klin. (Berlin), 1920, **16**, 108.

Data published elsewhere. See Endocrin., **4**, 160.

(THYROID) Goiter and "old tuberculin" (Struma und Alttuberkulin). Althen, München. med. Wchnschr., 1920, **67**, 651.

Goiter and Graves' disease are remarkably often combined with tuberculosis. Therefore the author tried to cure goiter with local application of Koch's "old tuberculin." Every three days he rubs the left arm, the left part of the thorax, the right part of the thorax, the right arm and the skin over goiter with one drop of tuberculin. Often after one treatment the goiter becomes smaller. If after one series no success is seen, a second one is tried, but at the same time twice daily 10 drops of "jodvason" are rubbed on the goiter.—J. K.

THYROID Hormone, Action of the— (Die Wirkungen des Schilddrüsenhormons). Asher (L.). Therapeutische Halbmonatshefte (Berlin), 1920, **34**, 221-224.

A general review. Iodothyrin is not able to replace the hormone of the thyroid. Oswald's thyreoglobin, however, can take the place of this hormone. It has not been settled as yet whether this is possible with Kendall's thyrotoxin.—J. K.

(THYROID) Problems relative to prophylaxis of rural endemics in Brazil (Algunos problemas relativos a profilaxia de endemias ruraes no Brazil). Cruz' and Chagas' disease (Molestia de Cruz e Chagas), Vasconcellos (F.), Soc. de Med. e Cirugia de Rio Janeiro, July 15, 1919.

Chagas' disease was discussed in important papers by two disciples of Oswaldo Cruz. F. V. affirmed that the Trypanosoma cruzi was discovered personally by Oswaldo Cruz, and that for this reason the Brazilian trypanosomiasis should be called Cruz' and Chagas' disease rather than by the name merely of the latter. The two authors were in agreement that the pathogenic importance of the disease might seem to have been exaggerated were it not known that 29 well veri-

fied cases have occurred and these in acute form in young infants. It is true that diagnoses of the chronic form have often been made also by the finding of pulmonary cysts in guinea pigs into which blood of the patients had been injected, but it has been demonstrated that these pneumocysts may be found in guinea pigs not injected at all, and that they are due to another organism than the protozoon in question. Both authors maintain that it has not been proven that endemic goitre is due to the trypanosome, and they agree with Kraus, Maggio and Rosenbusch that there has been a confusion of two diseases existing in the same district. It is certain that these restrictions oblige a renewed study of the chronic form of the disease but do not detract at all from the interest in the masterly study which Chagas has made of the acute form.—B. A. H.

(THYROID-PARATHYROID) On the effects of thyro-parathyroidectomy in the castrated guinea pig (Sur les effets de le thyroparathyroïdectomy chez les cobaye chatré). Athias (M.) & Ferreira de Mira, Compt, rend. Soc. de biol (Paris), 1920, **83,** 876-877.

The aim of these experiments was to see if castration in the guinea pig had any effect on the results of thryoparathyroidectomy. Previous results by various workers have been conflicting. Eight males over 3 years of age that had been castrated at the age of one or two months, and three females castrated three and a half months previously were the material used, with one male and two females over 4 years old (normal) as controls. All the animals died after removal of the thyroparathyroid apparatus, the time of death varying between one and seventy-three days, the symptoms in the castrated animals being the same as in the uncastrated controls. The conclusion is reached that castration does not preserve the guinea pig from the fatal results of thyroparathyroidectomy.

The THYROID in infections. Barbara (M.), Annali di Clinica Medica (Palermo), 1919, **9,** 1-20.

Data reported elsewhere. See Endocrin., **4,** 93-94.

(THYROID) A preliminary report on the endocrine therapy of high blood pressure. Bandler (S. W.), N. Y. Med. J. (N. Y.), 1920, **111,** 972-974.

A brief report of seven cases of high blood pressure which responded favorably to thyroid extracts. No change of diet

was made in ambulatory cases. No teeth were pulled or tonsils removed.—H. W.

(THYROID) Goitre in an infant. Barnett (E. C.), N. Zealand M. J. (Wellington), 1917, **16,** 143.

In an infant five weeks of age the thyroid was enormously enlarged, threatening asphixia. At operation the isthumus was resected with a view particularly to forestalling asphixia. The results were excellent. The child's weight began at once to increase. The enlargement of the lobes of the thyroid gradually disappared and has not recurred. At the time of writing the child was perfectly well.—R. G. H.

(THYROID) Hereditary occurrence of hypothyroidism with dystrophies of the nails and hair. Barrett (A. M.), Arch. Neurol. & Psychiat. (Chicago), 1919, **2,** 628-637.

Barrett reports the case of a patient showing the disorder mentioned in the caption in whose family history for generations have occurred trophic disorders of the nails and hair together with various mental and nervous disorders. In case of the patient reported the skin felt somewhat thickened and there was puffiness under the eyes. The hands were pudgy and the fingers short and clubbed. The hands and feet showed cyanosis. The hair of both the head and body was scanty. The eyebrows consisted of but a few short stubby hairs. The nails of both fingers and toes were short, failing to reach by a quarter of an inch the ends of the digits. No lanula was present. The ends of the nails were thickened and broken, though the nail surface was smooth. The skin was dry and at the ends of the digits tended to exfoliate. The patient was subject to tics of the face and shoulder. Speech was thick and nasal. Bone conduction was lacking for the left ear. There was marked hyperopia. Thyroid medication resulted in marked improvement. Similar deficiencies had occurred in the family for at least six generations. Among 61 members both hair and nails were affected in 14 instances. The nail defect seemed to be about the same in all, but there was much variation in the degrees of loss of head hair. In the greater number there was an extreme scantiness as to the amount of hair. In no instance was there a total loss of all hair of the head, the most extreme cases showing a fine lanugo-like covering of the scalp. Aside from this particular abnormality there were other features that showed that in this family group there were conditions active in the production of a variety of disorders that are of much interest to neuropsychiatry. This is the high frequency of feeblemindedness and

neurologic disorders of a degenerate type among the family. The members of the third generation who had dystrophies of nails and hair, and all of their descendants, numbered 29 persons. Of these, 22 were definitely abnormal. Twelve of the latter had the characteristic family dystrophy, and 10 others, who lacked this, showed other constitutional and nervous disorders. These included one case of epilepsy, one of hysteria, one of severe tic, four instances of feeblemindedness, one of nocturnal enuresis and four died at an early age from marasmus. Even those who had the nail and hair dystrophy had other abnormalities. One of these was an epileptic; one had cancer; four were feebleminded, and one had nocturnal enuresis. The well known association of abnormalities of hair and of nails in hypothyroidism, and two fairly well defined cases of juvenile myxedema which led to this study, and the reaction of one patient to thyroid feeding, seems to warrant in Barrett's opinion the conclusion that the fundamental disorder in this family was of the thyroid gland.

A review of the literature discloses a number of other families with a similar history to that cited. A summary of these is included.—R. G. H.

(THYROID) Subtotal thyroidectomy. Bartlett (W.), Surg. Gynec. & Obst. (Chicago), 1917, **25,** 402-410.

The article is largely of technical interest, giving many details of operative procedure. The desirability of taking away most of both lobes of the thyroid (in exophthalmic goitre) is stressed. A small proportion of the gland, the amount depending upon the individual conditions, should be left. In twenty-six cases upon which the method was practiced the results were "practically ideal."—R. G. H.

(THYROID) Preliminary report on a new method for the clinical diagnosis of toxic thyroid states, with a note on serological technique. Berkeley (W. N.) & Koopman(J.), Med. Rec. (N. Y.), 1920, **97,** 1035-1037.

Using normal dog thyroid as antigen, Berkeley tested 175 human sera of which 40 were from patients with suspected thyroid diseases; 18 of the 40 were undoubted instances of Graves' disease and gave positive complement fixation response. Control serums in 135 cases gave negative results in all except one. Furthermore, as the positive Graves' disease patients improved under treatment the test changed from four plus to two plus, etc. The test has been repeated hundreds of times and has been checked carefully with controls. The author hopes it will prove of value in differentiating per-

plexing cases from true hyperthyroidism and will aid in judging the effects of treatment. Dog thyroid would seem to contain a substance native in the dog but toxic in man. This substance Berkeley calls cynothyrotoxin and presumes that it is formed in the human thyroid under the abnormal chemical conditions which appear when exophthalmic goitre develops. The antigen is an extract of the mixed thyroids of five or six dogs. It slowly deteriorates and a fresh supply must be obtained in three weeks. Details of preparing the antigen are given.—H. L.

Carcinoma of the THYROID. Blaxland (A. J.), Brit. M. J. (London), 1920, (i), 454.

In the writer's experience adeno-carcinoma of the thyroid is rare, and a correct diagnosis is not usually made until the growth has spread through the capsule of the thyroid and the chance of cure by operation is remote. He cites a case occurring in a woman of 25. The lobe in which the tumor was situated was removed without difficulty and the diagnosis was made on microscopical examination. This patient had had the other lobe of the thyroid removed six years previously for parenchymatous enlargement.—L. G. K.

(THYROID) A case of goitre with nearly total external ophthalmoplegia (Een geval van struma met ophthalmoplegia quasi totalis externa). den Boer (M.), Nederl. Tijdschr. v. Geneesk. (Haarlem), 1920, **64** (I), 2284-2286.

A woman of 34 with Graves' disease was operated upon. Ten years later she developed recrudescence of goiter with ptosis of both eyelids and paresis of the eye muscles, paresis of the levator palatina dextra and hemiplegia laryngis sinistra. The pulse was 70; there were no tremors and no hyperhydrosis, i. e., there were no symptoms now of Graves' disease. A combination of simple goitre and paralysis of the muscles mentioned above has never previously been described.—J. K.

THYROID, Hemorrhagic syndrome cured by thyroidin (Syndrome hemorragique guéri par la thyroïdine). Bottaro (L. P.) & Mussio Fournier (J. C.), Anales de la Fac. de Med. (Montevideo), 1920, **5**, 191-194.

See Endocrin., 1920, **4**, 366-368.

(THYROIDS PARYTHYROIDS) The effect of thyro-parathyroidectomy on the heart and circulation. Part II. Ac-

tion of guanidin on the heart of the frog. Burns (D.) & Watson (A.), J. Physiol. (Lond.), 1920, **53**, 386-390.

This work was undertaken to determine whether the nicotine-like action of guanidin afforded sufficient explanation for the circulatory disturbances following parathyroidectomy. Heart tracings taken after administration of guanidin compared with those taken before almost invariably showed cardiac retardation, whether the guanidin was injected into the dorsal sac, or painted on the heart, or the heart bathed in solution. Two causes for the retardation have been adduced: (a) Stimulation of the vago-cardiac nerves, and (b) pronounced vaso-constriction with reflex inhibition. There was a primary acceleration probably due to stimulation of the accelerator nerves of the heart. By the use of atropine and nicotine the point of action of guanidin has been localized. It has a nicotine-like action on the sympathetic neurons.—T. C. B.

(THYROID) Maladies and medicines. Campbell (Arthur), Practitioner (Lond.), 1920, **104**, 305-312.

The article consists of brief notes about sundry diseases and drugs. The author describes the first case of myxedema he saw, which was in 1883, a few days before the disease was first described. He mentions a case of Charcot's latent exophthalmic goitre.—H. L.

(THYROID) Basedow's disease accompanied by hypertrophy of the eyelids and cheeks (Maladie de Basedow avec hypertrophie des paupières et des joues). Chauffard (A.) & Monnot (P.), Bull. et mem. Soc. med. d. hôp. (Paris), 1917, 3. s., **41**, 421-423; 482-484.

Report of an interesting coincidence of Basedow's disease and hypertrophy of the eyelids and lips not oedematous in character.—F. S. H.

(THYROID) Goitre in pregnancy. Crotti (A.), Am. J. Obst. (N. Y.), 1917, **75**, 450-455.

Data published elsewhere. See Endocrin., **3**, 105.

(THYROID) The somatic causes of psychoneuroses. Dana (Charles L.), J. Am. M. Ass. (Chicago), 1920, **74**, 1139-1143.

The case is reported of a boy, aged 19, with a well marked psychoneurosis. He was subject to "seizures" of a peculiar sort. He would suddenly feel as if there were a burning, torturing fluid in his head and pouring through his body. After

a short time this feeling was superseded by nervousness, restlessness and apprehension. He finally had to give up all attempts at educational work. He succeeded no better at farm work. When seen by Dana he had been for four years nervous, hysterical and entirely lacking in courage or capacity to carry on any sort of work. His habits were good, as were his intelligence, affection and desire for recovery. There were no objective signs of nervous disease nor stigmata of schizophrenia. The physical description given does not point to any definite endocrine anomaly unless a dry skin and subnormal temperature be taken to indicate such. He was put on thyroid treatment, ten, and later, four grains a day. "Within two weeks after treatment was begun the boy was rather magically changed. He lost his fears and restlessness, and nervousness and insomnia. He was able to go out alone. He went back to his work and became practically well and continued so for nearly three years." He takes thyroid intermittently when he notes a tendency of the nervous symptoms to return and gets entire relief. The author refrains from endocrine theorizing on the case.—R. G. H.

A case of INFANTILISM. Elmslie (R. C.), Brit. J. Child. Dis. (Lond.), 1920, **17**, 39.

Report of a case occurring in a girl aged 15 years and 10 months, whose height was 3 feet. Skiagrams of the wrists showed cupping of the ends of the diaphyses with widening of the epiphyseal cartilages as in rickets, while the hips showed coxa vara of the rachitic type. Sexual development was absent, breasts undeveloped, pubic hair absent and menstruation not yet begun. Albuminuria and chronic intestinal trouble were present. No studies were made of the general metabolism. From the description it appears as if the condition were due to a combined dysfunction of the thyroid, pituitary and sexual glands.—M. B. G.

(THYROID OVARY) Polyglandular syndrome with late epilepsy (Un nouveau cas de syndrome polyglandulaire avec épilepsie tardive). Etienne (G). & Richard (G.), Bull. et mem. Soc. méd. d. hôp. (Paris), 1920, 3. s., **44**, 154-158.

The authors report the case of a woman of 32 who had for the past three years suffered with generalized convulsions which appeared on the second or third day of each menstrual period. The periods were much reduced. The seizures stopped at once under combined thyroid-ovarian therapy, but for a time there were epileptic equivalents. The patient was clearly

sympathicotonic. The seizures were explained as due to spasms of the cerebral blood vessels which were regarded as due to thyroid-ovarian insufficiency. (The reviewer noted several years ago that ovarian extirpation in experimental animals leads to augmented irritability of the sympathetic nervous system.) (See also Tracy, Endocrin., **4**, 221.)—R. G. H.

(THYROID) A case of acute senile hyperthyroidism (Un caso de hipertiroidismo). Fernandez Sanz (E.), Anales de la Real Acad. de med. de Madrid, May, 1917.

A female subject of 82 suddenly exhibited a most acute Basedow syndrome. At this age hyperthyroidism always has a menacing prognosis, but this subject was entirely cured by medical treatment.—G. M.

(THYROID) The treatment of goiter. Foss (H. L.), N. Y. Med. J. (N. Y.), 1920, **111**, 285-286.

A defense of surgical procedure in the treatment of goiters, especially the exophthalmic forms.—H. W.

(THYROID) The principles underlying the treatment of toxic goitre. Frazier (Charles H.), Penn. M. J. (Athens, Pa.), 1920, **23**, 437-444.

Frazier emphasizes our ignorance of the etiology of toxic goitre. In stressing the importance of the thyroid gland he alludes to: (1) the disturbances related to its influence on the vegetative or sympathetic nervous system; (2) the visceral disturbances as represented by the vagotonic and sympathecotonic types; (3) the symptoms related to disorders of the central nervous system; (4) the disturbances of growth as in cretins, the alterations in the skin, etc., and (5) the disturbances arising from the relationship of the thyroid to the other glands of internal secretion. The author classifies toxic goitre patients into five groups. (1) The mildly toxic of the adolescent group rarely require surgery. (2) In the mildly toxic of the adenoma group operation is usually a matter of choice and not of necessity. (3) In the grave toxicosis of the adenomata, not the true exophthalmic type, but often with as grave an outlook, operation is inevitable, according to Frazier. (4) In the initial hyperplastic goitre without a pre-existing adenoma, the author is a very positive advocate of operation,—the earlier the better. (5) In the degenerative or atrophic or terminal stage of a more or less prolonged hyperthyroidism, there is manifestly no justification for surgery. In determining the

toxicity of a given case, basal-metabolism and blood sugar tests are valuable but should never be the sole criteria on which to depend; other objective and subjective signs must be taken equally into consideration, weighed and balanced. Frazier is an enthusiastic advocate of nitrous oxide anesthesia in toxic goitre operations. If ligation is done it should include the superior pole and not merely the superior thyroid artery. The author's mortality has been 3.5 per cent.

(Frazier's article and Goetsch's article abstracted in this issue were read before the Pennsylvania State Medical Society and an interesting discussion by several clinicians, including Plummer, is also published at the close of Frazier's paper.)

—H. L.

(THYROID) "Epinephrin hypersensitiveness test" in the diagnosis of hyperthyroidism. Goetsch (Emil), Penn. M. J. (Athens, Pa.), 1920, **23**, 431-437.

The author prefaces his article by reference to the work of Eppinger, Falta, Rudinger, Hess, Oswald, Cannon, etc., in demonstrating that excessive thyroid secretion renders the sympathetic nervous system sensitive to the action of epinephrin. He then describes in detail the technique of his "Epinephrin hypersensitiveness test." The test may result in considerable exacerbation of the objective signs and symptoms with but moderate increase of subjective phenomenon, or vice versa. Either combination would be considered positive. His conclusions are based on a clinical study of approximately 300 cases of thyroid disease. Goetsch finds the test definitely positive in cases of exophthalmic goitre; negative in colloid goitre cases without symptoms of hyperthyroidism and mildly or moderately positive when increased thyroid secretion prevails. In toxic adenoma the test is positive, in non-toxic adenomata negative. The test is helpful in differentiating incipient tuberculosis from mild hyperthyroidism in which, clinically, the diagnosis may be difficult; in the former there is no response to epinephrin, while in the latter the reaction is positive. The author attaches considerable importance to this phenomenon. He recommends the use of the test also in differentiating other conditions simulating hyperthyroidism such as psychasthenia, psychoneurosis, hysteria, neurasthenia, dementia precox, alcoholism, tabagism, acromegaly, arteriosclerosis and several other diseases. Furthermore, he believes the test of value in estimating the degree of toxicity in a given case of hyperthyroidism, and also finds that improvement in the response to epinephrin

(that is, a less positive reaction) runs parallel with decreased toxicity. The test also has the advantages of simplicity in apparatus and technique and is inexpensive.

THYROID, Metastatic abscesses of the—associated with hyperthyroidism; report of a case following repeated attacks of sore throat. Greenburg (David), J. Am. M. Ass. (Chicago), 1920, **74**, 165.

A report of a case of exophthalmic goitre, preceded by repeated peritonsillar abscesses and streptococcus sore throat. The author believes that bacteria may be a factor in the causation of exophthalmic goitre, if not directly, at least by effecting such changes in the physiology of the gland as to make its appearance likely.—F. C. P.

(THYROID) Sporadic cretinism (Ueber sporadischem Kretinismus). Guleke. München. med. Wchnschr., 1920, **67**, 734.

Two cases. A deaf mute boy of 13 showed some spontaneous improvement without treatment. Perhaps there was some spontaneous new formation of thyroid. In a second case, a girl of 16, three pieces of fresh thyroid were implanted without marked success.—J. K.

(THYROID) Morphologically demonstrable fat substances and the oxidase reaction in the human thyroid. Haeberli (E.), Arch. f. path. Anat., etc. (Berl.), 1916, **221**, 333-351.

In young individuals the fat content of the thyroid consists largely of neutral fats, i. e., fatty acid esters of glycerol. Thyroids of older individuals contain mainly neutral fats; cholesterol esters are seldom found, free cholesterol never. Microchemical staining reactions may lead to errors in the chemical differentiation of lipins. The granules in the epithelial cells of the thyroid, as those in other epithelial cells, consist of a variety of substances, among which are fat and pigment. The fat in the epithelial cells is permanent fat and increases with age. Fresh thyroids constantly contain oxidase granules within the epithelial cells. These granules are closely associated with the stored fat. Chem. Abst. **14**, 2023.

Investigations on the THYROID gland (Part II). Horisawa (H.), Verhandl. d. jap. path. Gesellsch, 1919, pp. 54-57.

The author has made a study of the size and weight of the fresh thyroid gland in 529 individuals of different ages and of

the formalin fixed gland in 401 more. In males between 26 and 42 years old it weighs on an average 17.47 gms. and in females between 20 and 33 years of age, 15.30 gms. In 223 cases he gives also the percentage of thyroid to body weight. If detailed observations were made regarding the cause of death, anatomical variations in the gland, incidence of goitre in the vicinity, etc., this contribution should be one of considerable value.—E. V. C.

THYROID extirpation in the horse (La tiroidectomia en los caballos). Houssay (B. A.), & Hug (E.), Soc. de Biol. de Buenos Aires, May 6, 1920.

The experimental series included eight animals. These were observed for a period of five years. Thyroidectomy resulted in death with cachexia in three cases, retardation of growth in case of young animals, with synovial edema, retardation of sexual development, hypothermia, etc.—B. A. H.

(THYROID) Experimental goitre produced by water from Cerrillos (Bocio experimental provocado por el agua de Cerrillos). Houssay (B. A.), Soc. de Biol. de Buenos Aires, May 6, 1920.

Goitre was observed in rats that had drunk of this water. This is the first instance of experimental goitre reported from South America.—Author's Abst.

THYROID GLAND, Papilliferous carcinoma of the—. Hughes (B.), Brit. M. J. (Lond.), 1920 **(i),** 362-363.

The patient was a girl of 13 years. The papilliferous carcinoma which was removed at operation was of 10 months' duration and involved the right lobe of the thyroid gland and some of the lymphatic glands on the right side of the neck and was also adherent to the trachea and to the carotid sheath. At the time the paper was written, three months after the operaion, there was no sign of recurrence. The condition is extremely rare, especially in children. The papilliferous form is far less malignant than the ordinary carcinomata, the history often extending over years. These tumors show little tendency to infiltrate; the metastases are local and situated in the glands of the neck, and they may appear years after the removal of the original growth. The affected glands remain movable and discrete and their removal is easily accomplished. The original tumor, if removed before infiltration has occurred, shows little tendency to recur.—L. G. K.

Carcinoma of the THYROID. Hughes (B.), Brit. M. J. (London), 1920, **(i)**, 586.

The author states that he has never seen a case of adenocarcinoma of the thyroid gland in which operation could be definitely said to have effected a cure. The early involvement of the trachea and surrounding structures as the growth becomes extracapsular makes operation extremely difficult. The earliest symptom may be cough and blood stained expectoration caused by ulceration of the growth into the trachea.

—L. G. K.

(THYROID) Nerve block anesthesia in superior thyroid pole ligation. Hunt (J.), Northwest Med. (Seattle), 1920, **19**, 49-50.

The author describes a method of nerve block sufficient to permit superior pole ligation and recommends it for the reasons that time is saved by blocking before starting the operation, since infiltration does not produce sufficient anaesthesia under twenty to thirty minutes; that shock is lessened, and that better skin repair results when infiltration along the line of incision is not resorted to.—H. L.

(THYROID) Research on the artificial provocation of metamorphosis in batrachians, notably in axolotl. Biological measure of the efficacy of thyroid preparations (Recherches sur la provocation artificielle de la métamophose chez les batrachiens, et notamment chez l'axolotl. Mesure biologique de l'efficacité des préparations thyroïdes). Jensen (C. O.), Compt. rend. Soc. de biol. (Paris), 1920, **83**, 315-317.

The author has previously shown that intra-abdominal injections of iodothyrin determine metamorphosis in axolotl. Since then he has elaborated a method for measuring the action of iodothyrin and other thyroid preparations by determining the minimum dose necessary to provoke metamorphosis.

—T. C. B.

THYROID gland and anomalies of metamorphosis in the anura (La glande thyroïde et les anomalies de métamorphose chez les anoures). Jensen (C. O.), Compt. rend. Soc. de biol. (Paris), 1920, **83**, 948-949.

The author has studied the thyroid in specimens of Rana esculenta, R. arvalis and Bufo vulgaris that presented various anomalies with regard to metamorphosis. In a lot of Bufo

larvae three individuals metamorphosed very early. In these the thyroid was not hypertrophied, but the follices were filled with masses of colloid with a stronger affinity than normal for eosin. In the larvae of R. arvalis, of which the development was notably more advanced than that of the controls, the thyroid attained dimensions much greater than that of the control; the follicles were large and filled with colloid, but not proliferated. It is possible that the secretory activity of the thyroid had been more intense in these individuals than in the controls. In the larvae of R. esculenta that had passed the winter at a temperature of 6-10° the thyroid was found at the end of March very large on account of swelling; the follicles were filled with colloid having little affinity for eosin; the epithelium was very flat. Larvae of the same size and state of development, collected from the same pond, but killed in October, served as controls. Giant larvae of R. esculenta were also studied, and a histological description of the thyroid is given.

—T. C. B.

(THYROID) Endocrine tropisms: thyrotropism. Kaplan (D. M.), N. Y. Med. J. (N. Y.), 1920, **111**, 275-280.

This is one of a series of articles in which the author is attempting to show that every individual is dominated by the makeup of his endocrine system. According to the author, a thyrotrop may show his tropism in four different ways: an over action, an under action, a perversion of the secretion, or the first two may be present at the same time. The various findings under each condition establish the character of the individual possessing them. All thyroidal conditions cannot be ascribed to primary disturbances in the thyroid for the pathology of other endocrine organs results in a condition in which the thyroid attempting to compensate brings destruction upon itself. Hence the thyroid, as such, should not be held responsible until the functions of the other endocrine glands have been completely established, nor removed until organotherapy and modern medical procedures have been thoroughly applied. Many cases improve on ovarian extract, 5 grains a day, and hand in hand with their improvement goes a dermal condition analogous to acnea rosacea.

In some respects this "dominance of the endocrines" reminds one of the old theory of phrenology and especially of physiogomony dressed up in modern or "new thought." The manner of the author in "initiating" the reader into the secrets of endocrinology presupposes that the reader has scarcely heard of the wonders of the ductless glands.—H. W.

(THYMUS THYROID) Internal secretory organs in morbus Basedowii. Kato (M.), Verhandl. d. jap. path. Gesellsch, 1919, ——, 59.

On the basis of the study of ten cases of Graves' disease the author concludes that this condition is closely related to the so-called status thymicolymphaticus.—E. V. C.

Deficient THYROID secretion as an etiologic factor in gastric and duodenal ulcers and in hyperacid conditions. Katz (Joseph), Med. Rec. (N. Y.), 1920, **97**, 916.

Brief report of four cases, three of hyperacidity and one of gastric ulcer, which were strikingly improved by thyroid extract.—H. L.

(THYROID) Determination of iodine in connection with studies in thyroid activity. Third paper. Kendall (E. C.), J. Biol. Chem. (Balt.), 1920, **43**, 149-159.

A detailed description of the procedure to be followed for the accurate determination of iodine in amounts found in thyroid tissue.—F. S. H.

(THYROID) DIABETES and exopthalmic goiter (Diabéte et goitre exopthalmique). Labbé (M.), Ann. de méd. (Paris), 1920, **7**, 95-103.

After nothing that he has observed a coincidence of diabetes and Basedow's disease in five cases, but has never found myxedema associated with the former, the author gives brief protocols of the patients presenting the associated pancreatic and thyroidal disorders. The susceptibility of such patients to acidosis is partially attributable to the increased nitrogen metabolism induced by the hyperthyroidism.

Medication with hemato-ethyroidine and valerian and bromides gave little if any relief. Better results were obtained with quinine and sodium salicylate. Treatment with iodine preparations gave most favorable results both in lowering the glucosuria and in general amelioration.—F. S. H.

(THYROID) Loss of both eyes from the exopthalmos of hyperthyroidism. Lahey (F. H.), Boston M. & S. J., 1920, **182**, 427-428.

X-ray treatments resulted in a reduction of the pulse rate, a gain in weight and improvement of the general condition.

However, the exopthalmos continued to progress and ulcers of the right eye led to its enucleation. Later the left eye was removed for the same reasons after severance of the sympathetic cervical ganglion had failed to arrest the condition.
—H. W.

(THYROID) Metabolism as an aid in diagnosis, prognosis and treatment of hyperthyroidism. McGuire (Stuart), South Carolina M. Ass. J. (Greenville), 1920, **16**, 107-119.

McGuire believes that the determination of basal metabolism, although a very promising method, has not yet been sufficiently long in use to permit a final evaluation of its significance in the diagnosis of "hyperthyroidism."

A patient with hyperthyroidism may have a high metabolic rate and not be as seriously ill as another with a lower rate but who has structural changes in the heart, liver or kidneys. The onset of hyperthyroidism is insidious and difficult to recognize in its early stages in which the metabolic rate will clearly differentiate it from hysteria, neurasthenia, tuberculosis, and other conditions with which it may be confused. Again, in the later stages there develop symptoms due to degeneration of the heart, liver or kidneys, and it is difficult to say how much the patient suffers from hyperthyroidism and how much from damage to the vital organs. Here also a determination of the basal metabolism will be of value, not only for diagnosis but for prognosis as well. Usually, a patient's clinical symptoms coincide with his metabolic rate; but sometimes they do not. Patients with high metabolism and moderate tachycardia are more seriously ill than those with moderate metabolic increase and a very rapid heart action. In treating a patient for hyperthyroidism, the estimation of the metabolic rate is of value first to determine the safety of the measure to be employed, and second to ascertain its efficiency.—R. G. H.

(THYROID) Zur Lehre der STRUMA INTRATHORICA. Mayer (Karl), Zentralbl f. Chir. (Leipzig), 1919, **46**, 536.

Mayer found that X-ray photographs enabled a diagnosis to be made of intrathoracic goitre and enlarged thymus, although a dermoid cyst cannot be distinguished from the above. The retrosternal goitre may be a continuation of the goitre in the neck, but an intrathoracic goitre may exist without any enlargement of the gland in the neck. Moreover, accessory thyroids may be met with at any point in the line from the base of the tongue as far down as the front of the arch of the aorta

and pericardium, or even in the posterior mediastinum.—Med. Sc. Abst. & Rev., **1**, 173.

(THYROID) The treatment of early hyperthyroidism. Meredith (Florence L.), N. Y. Med. J. (N. Y.), 1920, **111**, 289-291.

The state of being generally below par leads to the acquiring of infections and to metabolic and secretory disturbances. In young women nonhygienic modes of living often result in thyroidal disturbances, hence the normalizing of the life of the individuals so affected is a logical procedure in the care of early hyperthyroidism. In thirty young women suffering from early hyperthyroidism marked improvement followed the establishment of a normal mode of living.—H. W.

(THYROID) Functional PANCREAS insufficiency. Moyer (A.), Ztschr. f. exp. Path. u. Therap., 1919, **20**, 273-297.

Disturbances of pancreatic function are a part of the aftermath of the war. The disorders are evidenced by fecal examinations after test meals, studies of individual specimens of pancreatic juice, etc. Gastric achylia and thyroid disturbance frequently accompany this functional perversion of secretion. There is apparently a gastrogenic, neurogenic, and thyreogenic complex bound up with the pancreas disturbance, which is fundamentally possibly connected with the type of nourishment ingested during the war.—F. S. H., Chem. Abst., **14**, 2027.

THYROID extract, The life history of the first case of myxoedema treated by—. Murray (G. R.), Brit. M. J. (Lond.), 1920, **(i)**, 359-360.

For data seen Editorial (p. 600) in this issue.

(THYROID) X-ray treatment of Graves' disease (Om Behandlingen af Mb. Basedowii). Nordentoft (S.), Ugesk. f. Læger (Copenhagen), 1919, **81**, 1169-1175.

In 1918 Nordentoft published fifty cases of Graves' disease treated with X-rays in the period July, 1915 to December, 1917. His present paper deals with a new series of fifty cases, only three of which were males. At the Aalborg Kommune Hospital the practice has been adopted of exposing only the region of the thymus to the X-rays. He gives a few illustrative cases, but does not attempt to tabulate or classify his results, confining his estimate to general terms. He is greatly impressed by the efficacy of this treatment, with which better results can be

achieved than with any other. He urges its adoption at an early stage before the disease has got well established, and he advocates large and few doses in preference to small and frequent doses. With the adoption of this principle, and the inclusion of the thymus in the area exposed, he anticipates that severe and fatal cases of Graves' disease will become so rare that many medical men will never see them. Discussing X-ray fatalities in connection with Graves' disease, he suggests that timid dosage may partly be responsible, and he quotes Forsell in support of his hypothesis that the small dose merely stimulates, whereas the large dose inhibits the activities of the thyroid. He also notes that in certain fatal cases of Graves' disease death probably occurred in spite of, not because of, the X-ray treatment.—Med. Sc. Abst. & Rev., **2**, 202.

(THYROID) Toxic goitre. O'Day (J. C.), N. Y. Med J. (N. Y.), 1920, **111**, 287-289.

The removal of each lobe of the thyroid gland in five cases did not give the slightest relief, hence something more than the hyperthyroidism is involved in toxic goitre. The injection of toxic goitres with mucin is of no avail as treatment, although mucin is supposed to be the material which infiltrates the body tissues in cases of myxedema. The cause of toxic goitre is not known.—H. W.

Bone tumors of THYROID origin. O'Day (J. C.), N. Y. Med. J. (N. Y.), 1920, **111**, 374-375.

The author believes that normal detached thyroid epithelial cells are self-asserting within two environments, namely, the bony tissue and the parent structure itself.—H. W.

(THYROID) Is endemic goiter a water disease? O'Day, (J. C.), N. Y. Med. J. (N. Y.), 1920, **111**, 634.

Areas of the United States where goiter is endemic in character without exception are supplied with water deficient in mineral content. Hence endemic goiter, which is always retentive goiter, is the result of the deleterious effects that mineral free water has on the consistency of the thyroid's secretion. This view is the direct opposite of the one previously held. The relation of water to goiter, if there is one, apparently remains to be solved.—H. W.

(THYROID) What is the cause of goiter? O'Day (J. C.), N. Y. Med. J. (N. Y.), 1920, **111**, 556.

Diffuse and nodular goiters may be assumed to arise because of obstruction of one or more of the few lymphatic trunks which drain the thyroid. Such an obstruction would mean the accumulation of secretion within the follicles until, one after the other, they would burst and fuse to form a large cavity with the cuboidal epithelial cells of each flung back to be compressed into the wall of the cyst. The cause of this interference in drainage may be either mechanical or physiological. The latter is due to some defect which permits the production of an over-thickened product too heavy and thick for easy egress. Hence, persons of nervous temperament readily fall victims to goiterous conditions. On the other hand, "lymphoid temperaments," Hawaiians, Polynesians, etc., do not demonstrate retentive goiters.—H. W.

(THYROID) Diabetes in association with toxic goiter. O'Day (J. C.), N. Y. Med. J. (N. Y.), 1920, **111,** 815-816.

Two cases of toxic goiter associated with diabetes had their carbohydrate tolerance restored following subtotal thyroidectomy. In one case the thyroid was injected with boiling water, a definite reduction of the sugar content keeping pace with the piecemeal cooking of the gland.—H. W.

(THYROID) Emotive exophthalmic goiter and hypertrophy of the parotids (Basedowisme post-émotionnel et hypertrophie des parotides). Railliet (G.), Bull. mem. Soc. med. hôp. (Paris), 1918, 3. s., **42,** 1151-1154.

A report of a case of a soldier who suffered contusions as the result of which Basedowian symptoms developed; these were accompanied by marked enlargements of the parotids.

—F. S. H.

(THYROID) Intestinal hemorrhages in a hemophilic Basedowian treated with serum from a rabbit in a state of anaphylaxis (Hémorragies intestinales chez un Basedowien hémophile. Traitement par le serum de lapin en état d' anaphylaxie). Raymond & Rouquier (A.), Bull. et mem. Soc. med. d. hôp. (Paris), 1920, 3. s., **44,** 485-487.

A report of a case of Basedow's disease in which intestinal hemorrhages occurred and were stopped by two injections of 10 cc. of rabbit serum from an animal in the anaphylactic state from horse serum injections.—F. S. H.

THYROID and PANCREAS, Giant cell sarcoma of—. van Rijssel (E. C.), Nederl. Tijdschr. v. Geneesk. (Haarlem), 1919, **63,** (ii), 2014-2024.

Correction of citation, Endocrin., **4,** 345.

(THYROID) Toxic goiter following epidemic influenza. Roeder (C. A.), Surg., Gyn. & Obstet. (Chicago), 1920, **30,** 357-358.

Our knowledge of the etiology of goiter has not kept pace with our methods of treatment, an empiricism accounting for the prevalence of various types of enlarged thyroids. All non-malignant goiters can be divided into (1) colloid, (2) adenomatous, and (3) hyperplastic, and are either toxic or non-toxic. This simplification of the classification we owe to Plummer and it has greatly cleared our vision of a previously hopelessly described pathological condition. The etiology concerns us more than the treatment, and every goiter indicates a lack of some form of prophylaxis. The thyroid may have very little connection with the other glands of internal secretion, as to date it is extremely rare to find a goiter, hypo- or hyper-plastic, with various abnormalities of other glands. The infectious theory has lately gained popularity, and rarely do we find any type of goiter without a suspicious pair of tonsils or alveolitis and no goiter has been properly treated without the eradication of such foci. The author reports eight cases of toxic goiter (three adenomata and five hyperplastic) following immediately on the attack of epidemic influenza; the toxemia from the goiter succeeded the attack of influenza so closely that recovery from the latter was not complete before the symptoms of thyrotoxicosis began. There had been no toxic signs or symptoms from the thyroid previously. The close relationship between the two conditions is so marked that it can be accepted as a most convincing proof of the etiological factor being bacterial. At the time this abstract is being written the same author has observed fifteen cases all following epidemic influenza.—Author's Abst.

THYROID, Myxedema in total aplasia of the— (Ueber myxödem bei totaler Thyreoaplasie). Rössle, München. med. Wchnschr., 1920, **67,** 735.

Report of a post-mortem of a dwarf of 28. No trace of thyroid could be detected. The skeleton was formed as in a child of 4; there was a diminished endochondrial and periosteal ossification. Arteriosclerosis, especially of the aorta was seen.

The hair was poorly developed; the skin showed typical myxedema. The uterus and ovaries were as in a normal woman of 28. Only one parathyroid was found. The hypophysis was large (725 milligrams). The thymus consisted only of fat. The pineal, pancreas and spleen were normal. The zona glomerulosa of the adrenals showed a marked sclerosis.—J. K.

(THYROID ADRENAL) Fluctuations of thyrosuprarenal activity in general diseases. Sajous (C. E. de M.), N. Y. Med J. (N. Y.), 1920, **111**, 265-269.

Such diseases as pneumonia of the aged, dementia precox, influenza and the like represent failures of metabolism the result of toxins which affect the endocrine or defensive organs. Such diseases, therefore, should be treated along the lines of organotherapy, especially with adrenal and thyroid preparations.—H. W.

(THYROID) Urinary incontinence of hypothyroid origin (La incontinencia de orina en el hipotiroidisma). Salgado (A. A.), Innaug. Dissertation, Santiago de Chili, 1918.

Urinary incontinence of hypothyroid origin is definitely recognized by many authors; in such cases thyroid preparations constantly give favorable results. Salgado reports seven cases of this sort. In his experience those cases of enuresis that are accompanied by fecal incontinence are always due to chronic benign hypothyroidism.

[The problem of the relation of endocrine conditions to the physiology of the sphincters could profitably receive careful and extensive experimental investigation.—Ed.]—J. R. P.

(THYROID) The selection of operation for exophthalmic goiter. Sistrunk (W. E.), J. Am. M. Ass. (Chicago), 1920, **74**, 306-308.

Of technical surgical interest.—F. C. P.

(THYROID) Goiter in skiagrams (Der kropf in Röntgenbild). Sommer. Deutsche med. Wchnschr. (Berlin), 1920, **46**, 616.

Of no endocrine interest.—J. K.

THYROIDAL constipation. Strauss (S. G.), N. Y. Med. J. (N. Y.), 1920, **111**, 281-283.

The establishment of thyroid deficiency with constipation is an indication for thyroid therapy. Doses of from 1/10

to 2 grains may be used without other cathartics until recovery is complete.—H. W.

(THYROID) Comparative investigations on the changes in the thyroid in different diseases. Takeuchi (K.), Verhandl. d. jap. path. Gesellsch., 1919, p. 58.

The author advances the following conclusions on the basis of his study of the thyroid in 325 cases: (1) The "thyroiditis simplex" of de Quervein, which consists chiefly of abundant desquamation of the epithelial cells and reduction in the amount of colloid substance, is not, as he supposed, specific for infectious diseases, for these appearances are less apparent in typhus abdominalis and spirochaetosis icterohemorrhagica than in non-infectious diseases. (2) Since these changes are more apparent in heart failure, diseases of the larger blood vessels, nephritis and cirrhosis and cancer of the liver, he is of the opinion that there is some connection between changes in the thyroid and alterations in the circulatory system. (3) In tuberculosis, malignant tumors, etc., the thyroid is more affected when the chief lesions are present in the thorax, which indicates a further connection between changes in the thyroid and the organs of the chest.—E. V. C.

(THYROID) On the influence of complete thyroidectomy during pregnancy upon the development of the fetus and on the duration of gestation. Ukita (T.), Acta Scholae Med. Univ. Imp. in Kioto, 1919, **3**, 287-297.

This report is based upon a study of the effect of thyroidectomy in six pregnant rabbits. Unfortunately no narcosis was used. Assuming that the thyroid gland begins to function in the fetus after the middle of gestation, the operations were performed between the seventh and tenth days after conception, in order to obtain the maximum effect. Maternal thyroidectomy immediately disturbs the development of the fetus in utero. The duration of pregnancy is nearly doubled and the young at birth are small and weak with hypertrophied thyroids and show retardation in development of their centers of ossification. The author believes, with Halsted, that the increase in the size of the thyroids is compensatory to the maternal thyroidectomy. The article is in English.—E. V. C.

(THYROID HYPOPHYSIS) The interpretation of headache. Wilson (W.), Practitioner, 1919, **103**, 274-296.

Among other causes of headache, the author mentions menstrual and climacteric headaches the mechanism of which he finds difficult to explain. He refers also to headache associated with hypothyroidism and relieved by thyroid extract; headache due to pituitary affections and usually occurring early in the disease before any obvious change in skeletal structures. The pain is situated deep in the head behind the root of the nostrils at the site of the sphenoidal sinus. These pituitary headaches are intermittent and the patient is quite prostrated. Relief from the attack is quite sudden. He considers these patients suffer from diminished pituitary activity and relief is obtained by administration of whole gland pituitary extract provided there is no malignant growth or spreading cyst.—H. L.

(THYROID) A comparison of methods for determining thyrotoxicosis. Woodbury (M. S.), J. Am. Ass. (Chicago), 1920, **74**, 997-999.

A report of the observation of a selected group of eleven cases of thyrotoxicosis by clinical study, by histological examination of the thyroids removed at operation, and by postoperative progress. The clinical observations included a careful history, the response to Goetsch's epinephrin chloride test and a study of the basal metabolic rate as determined by oxygen consumption (Benedict portable apparatus). Woodbury states that while the epinephrin chloride test is generally conceded to be essentially an indicater of hypersensitiveness of the sympathetic system, it appears to be a fact that positive responses to the test are more common in cases in which there is thyrotoxicosis. The test should be used especially in doubtful cases since it stimulates closer study and offers additional aid in formulating a diagnosis. Observations of the level of basal metabolism alone, as now estimated, should not be regarded as sufficient criteria in determining the presence or absence of toxic states associated with the thyroid. The author concludes that while functional tests are of great value in the compilation of evidence, especially in relation to the degree of toxicity, reliance should not be placed on any one of these. The diagnosis should be based on the results of a complete examination, with special attention to the possibilities of errors in psychoneurotic patients.—F. C. P.

Endocrinogenic VISCEROPTOSIS (Les ptosis hormónicas). Quaristi (V.), Prog. de la Clinica (Madrid), 1918, ——, ——.

In addition to visceral ptoses due to mechanical disturbances, such as genital prolapse in women who have borne

many children and suffered from lacerations and relaxations, the author believes there are others manifested in young persons which are due to endocrine alterations. Among such are: (1) Visceral dislocation due to spasms or ptosis; (2) Vascular disturbance, varix, etc.; (3) Neuroses. These three symptoms are exhibited most clearly in varicocele and rectal prolapse. There exist, moreover, genital prolapse, nephroptosis and gastroventeroptosis, in addition, and in all these cases we speak of consecutive neuroses. It is the author's opinion that these disturbances ought to be regarded as coexistent, and that they are due to lack of muscular and vascular tone. This being determined the cause is to be sought in the endocrine and vegetative systems, especially in suprarenal and hypophyseal insufficiency. The rational treatment of these conditions is opotherapy.—E. B.

(VAGOTONIA SYMPATHICOTONIA) Experiments on the influence of the involuntary nervous system on the blood (Untersuchungen zum Einflusz des vegetativen Nervensystems auf das Blutbild). Friedbery, Deutsche med. Wchnschr. (Berlin), 1920, **46**, 480.

Drug injections were made in children. It is not enough to examine the blood-picture of clinical cases of vagotonia or sympathicotonia, but the involuntary nervous system must be stimulated artificially and the blood-picture must be examined after this stimulation. It was observed that after stimulating the vagus with pilocarpin, depressing it with atropine or stimulating the sympathic with adrenalin the blood-pictures were practially identical. This is a strong argument against Falta's theory of the existence of a vagotonic and a sympathotonic blood-picture. The action of pilocarpin and adrenalin on the blood has probably nothing to do with the nervous system but is due to an influence on the hematopoietic organs.

—J. K.

Acute and chronic VAGOTONIA (Ueber aktute und chronische Vagotonie). Feilchenfeld (Leopold), Deutsche med. Wchnschr. (Berlin), 1920, **46**, 627-629.

The author makes the following classification:

I. Acute vagotonia with spasms of vagal origin; in these cases patients are women and usually hysterical. They suffer from fits beginning with shivering, headache, giddiness, nausea and vomiting. Often loss of consciousness is observed; the patients are pale; the pulse is slow.

II. Chronic vagotonia: In these cases physical stimuli may cause the attacks as described under I.

III. Paroxysmal tachycardia.

IV. Acute vagotonia in asthenocardia.

[It is a very old fact that a hysterical woman may have attacks and that diseases of the heart may give symptoms resembling those under I, but the evidence that they are due to vagotonia is by no means convincing.]—J. K.

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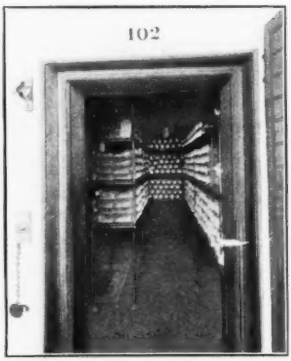

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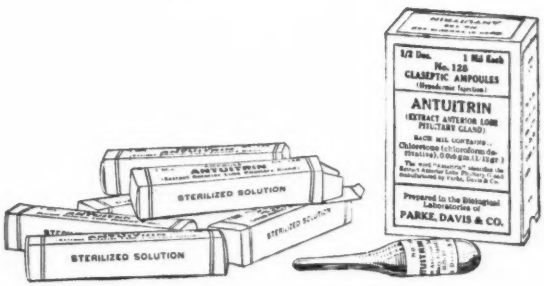

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